The Royal London

Ophthalmic Hospital Reports.

VOL. XVI. PART IV. JUNE, 1906.

ADDITIONAL CASES OF HEREDITARY CATARACT.

By E. NETTLESHIP.

SINCE the publication of a paper on hereditary cataract in the last number of these Reports, the particulars of several new cases have been sent to me by friends, and I have found the following published ones previously overlooked.

The classification of the cases is as nearly as possible the same as before, and the same signs are employed in the diagrams, viz.:—

♂, *Male.* ♂, *Male affected.*

♀ or ♀, *Female.* ♀ or ♀, *Female affected.*

○ or ●, *Sex not stated.*

◯, *Several siblings, i.e. brothers and sisters, unaffected;* if all are of same sex, the sex sign is added. A number within the circle indicates how many.

Parents joined by a bracket above, ♂ ♀, are cousins.

Twins are joined by a horizontal line above, ♂—♀.

A wavy line (~~) *beneath a childship* means that the order of birth is not known.

Successive generations are indicated by Roman numerals (I, II, &c.), at the side of the diagram.

The numbering of the cases and diagrams is continued from the last (Case 97, Fig. 45) of the previous series. The reference numbers are also continued from No. 52 of the last paper.

CLASS A. ACQUIRED OR POST-NATAL CATARACT.

I. *Senile.* CASE 98 (Fig. 46).—I regret that in my previous paper I omitted one of the most extensive recorded genealogies of hereditary cataract, that published

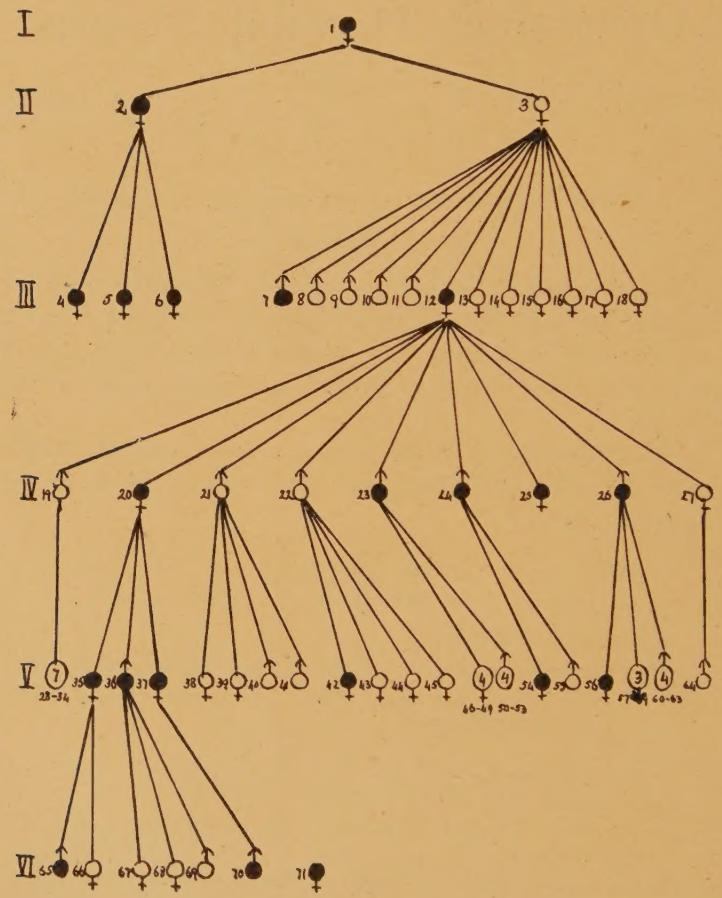


FIG. 46.

by Dr. John Green of St. Louis in 1890.[53] The pedigree is remarkable not only for its extent and the care with which it was worked out but for the strong evidence of "anticipation" (onset at an earlier age in each succeeding generation)

that it affords. I have kept the author's numbers for the various individuals.

Generation I.—(1) A woman who had cataract late in life. She had two daughters (*Generation II*, 2 and 3), of whom one (No. 2) also had cataract late in life. No. 3 appears to have been free.

Generation III, 4 to 6, three daughters of II, 2; all became cataractous late in life. 7 to 18, twelve children (five sons, seven daughters) of II, 3; the first-born (a son) had cataract late in life, the sixth (a daughter) showed signs of it at about 76, and when examined by Dr. Green in 1888 at the age of 83 had cataract complete in one eye, immature in the other. The other 10 children of II, 3, appear to have escaped.

In Generations IV, V, and VI, only the descendants of III, 12, were traced. III, 12, had nine children (IV, 19 to 27) of whom five (three male, two female) were affected, the cataract coming on between the 40th and 55th years of age. III, No. 12, and IV, 20 and 25, underwent extraction with good result.

In Generation V, containing 37 persons, there were six cases of cataract, and the disease is said to have appeared in all of them between 20 and 30 years of age. No. 37 was needled, but a well-defined nucleus coming forward into the a.c. within a few hours, linear extraction was performed (præsenile hard cataract); result excellent.

Generation VI seems to have consisted of only seven persons at the date of publication; three of the seven are known to have become affected between the ages of 6 and 9; all were treated by needling and solution, and obtained good vision. No. 35 (Generation V) was also treated by simple discission and did well, without evacuation of the lens. The exact parentage of VI, 71, was not noted, but she was the daughter of one of the females in Generation V, and her mother was said to have had perfect sight.

Of the 64 persons whose sex is stated 27 were males with 8 cases of cataract, 37 females with 14 cases, a relative excess of affected females over affected males in the proportion of 38 per cent. to 30 per cent. It will be noticed that though the descent was usually continuous, it was broken by an unaffected mother, No. 3 in Generation II, and by an unaffected father,

No. 22 in Generation IV; that in the offspring of these two, the proportion of affected to unaffected was small; and that of the 10 parents who transmitted the cataractous tendency, 7 were female, 3 male. As, however, the descendants of only one member of Generation III could be traced, the above figures are not conclusive.

CASE 99.—Senile cataract, anticipating and becoming præsenile; four generations involved. Additional case, communicated by Mr. J. Herbert Fisher (May, 1906).

Thomas Hawkins had early senile cataract at the age of 48 (1900); he also had glycosuria. His (Thomas Hawkins's) son, seen at the same time, had opacities in his R. lens (seen by Mr. Fisher).

His (Thomas Hawkins's) mother was operated for cataract at Oxford, and her father was also operated for cataract.

II. *Præsenile and Juvenile Cataract.*

Mr. E. C. Green, of Derby, sends me the following case.

CASE 100.—Father and mother healthy, with good eyes; issue six, of whom three have had præsenile cataract.

1. ♀ æt. 39 (1905), no cataract, but has been insane for a time.
2. ♀ Developed cataract rapidly at the age of 33; operated.
3. ♀ Cataract in one eye at 34, and six months later in the other; first eye operated, second eye not yet ready (1905).
4. ♀ Died in infancy.
5. ♀ Good eyes, married and has healthy children.
6. ♀ Cataract in both at 27, rapidly matured and operated.

The three girls with cataract were anæmic, prematurely aged, and intellectually dull, but none had grey hair. The opaque lenses were very white but not hard; all did well. No consanguinity of parents, and none known further back. Father was 12th of a childship of 15, married at 27 and died at 37; had good eyes. Mother was 3rd of 9, married at 26; still living, æt. 66, and sees well. None of the uncles, aunts or first cousins of the cataract patients have had cataract.

CASE 101.—Hall[54] in 1891 saw a man of 40, apparently a

native Indian, with complete cataract and "very opaque capsules," with evidence that the cataract had been present and progressing slowly for many years; one eye was operated with success. He brought three sons for examination, aged 18, 11, and 7, all showing "anterior polar cataracts in various stages of development."

Millikin[55] recorded the following in 1904.

Case 102, Fig. 47 (Author's Case 1).—Complete juvenile cataract in three generations. In Generation III, the first-born was a girl; cataract began in R. at æt. 9, and rapidly became complete; L. followed at æt. 13; both needled and did well.

Second, boy, cataract formed in both æt. 6; complete when seen at 8. One eye operated and did well. No other issue.

Generation II.—Mother operated successfully for cataract when a "girl." Her mother (Generation I) also operated successfully for cataract when "a young girl."

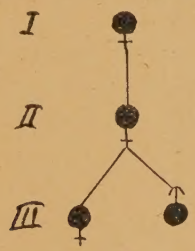


Fig. 47.

Schnabel[56] has published the following examples of heredity of cataract acquired in early childhood in two generations.

Case 103, Fig. 48 (Author's Case 3, Turi).—Father normal. Mother had double cataract removed by operation at the age of

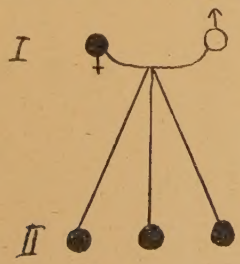


Fig. 48.

3 years with very good result; the cataract had appeared about six months before operation. Of her three children the eldest showed total soft cataract of L. eye at the age of 1½ years and was examined at æt. 8; the second had total soft cataract of L. at æt. 2 and was examined when 5; the third had total soft cataract of both at æt. 1 year and was examined when 2.

CASE 104.—In another case of Schnabel's (name not given) the father had been operated upon in childhood for cataract in both eyes with good result. Of his children (number not stated) two, who were born with normal eyes, developed cataract at 5 and 3 years old respectively.

CASE 105 (Fig. 49).—Schnabel's third case of this form of hereditary cataract (Gärtner family) is as follows:—

Generation I.—A woman, herself with normal eyes, was one of a childship of 6, of whom 3 became blind from cataract in early childhood; the parents had good eyes. This woman married twice, both husbands having good eyes. By 1st husband, 2 normal children; by 2nd husband 5 children, of whom 3 were blinded by cataract in both eyes in early childhood. (Sexes and order of birth not given.)

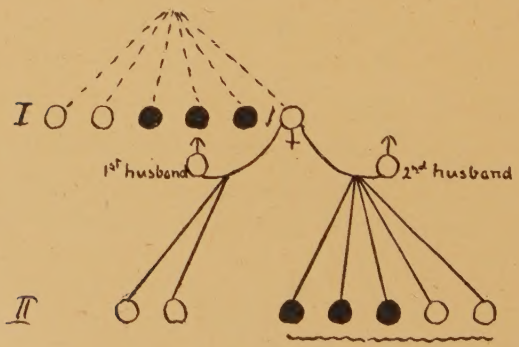


FIG. 49.

CASE 106, Nolte [57].—Case of juvenile complete cataract in one generation only.

Family of Debus. Parents have good eyes; no consanguinity. First-born, Maria, had some convulsions during her 2nd year;

between 5 and 6 sight began to fail; admitted when aged 7 with general nearly complete cataracts and shallow a. cs. (= swollen lenses); operation, good result. Second, George, born about 1 year after No. 1; scarlet fever and "typhus" when æt. 6; sight quite good till æt. 6, when it failed. Seen æt. 8 with double cataract L. complete, R. chiefly posterior cortex. No fits. Third, Johannes, born 7 years after No. 2; sight good until æt. 6½; when seen 6 months later (æt. 7) double general cataract, chiefly of anterior and posterior cortex, not zonular. History of a feverish illness lasting about a week some months before V. began to fail, and of otorrhæa soon after.

All three children appeared in good health when seen.

Case 107, from Mr. E. C. Green.—Father, an intelligent farmer, was operated upon for cataract in both eyes when æt. 9; he is now 48, and his eyes keep good. His four brothers and sisters all had good sight. No consanguinity between his parents nor between him and his wife. He has had only three children; all are living.

No. 1. ♂ Sight good till age of 5 years, when first R. then L. became cataractous, and were rapidly complete; needled. Robust and healthy.

2. ♂ Sight good till age of 5 years, when posterior polar cataracts began; became rapidly worse, and were needled. Robust and healthy.

3. ♀ Now (1906) æt. 6. Father reports her sight good.

B. CONGENITAL CATARACT.

I. *Lamellar Cataract.*

Case 108 (Fig. 50).—Mr. Herbert Fisher allows me to use the following important case of hereditary lamellar cataract from his practice at Moorfields, and I have to thank Mr. Payan Dawnay for much help in investigating the history. I have seen the notes of all the cases, and have examined all the five affected, and some of the unaffected, children in the third generation. I believe this case to be the most extensive of its kind on record.

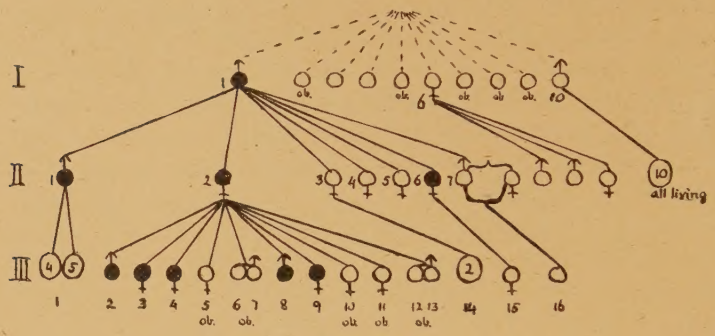


FIG. 50.

Generation I (1).—Charles Smith, now (1906) an old man, underwent discission by Mr. Bowman at Moorfields, first in one eye then in the other between the ages of 10 and 13 (1847, etc.). The entry in the Register on each occasion is "Congenital cataract." Many years afterwards a further needle operation was done by the late Mr. George Lawson for closed pupils and increased tension. He has now been totally blind for at least 15 years. He was the first-born of 10, of whom 5 died in early childhood and 5 (including himself) are living. All the living ones except No. 1 see well; the 6th (I, 6) is married and has 3 normal children, all living; the youngest, a Thames pilot (I, 10) has 10 children, all living and normal.

Generation II (1 to 7, children of I, 1).—No. 1, Charles T. Smith, told that he had cataract by the late Mr. George Lawson at æt. 18. Now æt. 40. Examined by Mr. Payan Dawnay April 28, 1906; dense lamellar cataract in each eye, the R. one showing a double shell of opacity; with R. reads 4/60, and 2 Jaeger at 8 inches.

No. 2, Emma, was operated for lamellar cataract at Moorfields in 1886 at the age of 18; she has recently had her loosened upper incisor teeth extracted; her lower incisors show imperfect enamel.

No. 6 (Florence) was also needled for lamellar cataract in 1886, when she was 9, and did well. Her first molar teeth were deficient in enamel. (Mr. Treacher Collins's note.)

I have examined No. 5, who was reported to have defective

sight, and found her lenses quite clear; eyes hypermetropic. The other 3 (II, 3, 4, 7) see well. No. 7 married a cousin, but has normal children.

Generation III has contained 24 persons. The first childship (III, 1) of 9 was the issue of II, 1, who has the cataract; the fifth was born dead; the first, second, third, and seventh died of measles, etc.; the fourth ♂ 11, sixth ♂ 8, eighth ♀ 7, and ninth ♀ 4 are living; I have recently examined them all, and found their lenses perfect. Only the eldest has permanent teeth, and they are normal. They are healthy, well grown children, and very intelligent.

The 2nd batch (Nos. 2 to 13) contains the children of II, 2, 10 births with 12 children (twins twice). Five are living, and I have seen them all; the first-born, William, third Emma, and seventh Edward, have been operated upon at Moorfields for lamellar cataract; whilst the second, Annie, æt. 14, and eighth, Lily, æt. 7, have typical lamellar cataracts and need operation (March, 1906). The fourth (III, 5) died at æt. 3 years; ninth (III, 10) died at 5 months, and was probably an idiot; the tenth (III, 11) died at 11 or 12 months. In each of the two twin-pregnancies, one miscarried at 4 months, the other (a boy in each instance) was born at full term; one of them dying at 5 months, the other at 12 months old. Thus every one of the 5 who were born alive and survived had lamellar cataract. In regard to the teeth of these 5 children, the permanent incisors are quite sound and well-shaped in all who have cut the permanent set (in the two youngest, III, 8 and 9, only the lower permanent incisors are up); the 1st permanent molars show deficiency of enamel in the two eldest (III, 2 and 3), but appear to me to be perfect in the other three (III, 4, 8, and 9). Some of the younger ones had convulsions. All the five living children are bright, intelligent, and well nourished, but the first and second-born are very undergrown.

In Generation I and the second-childship (2 to 13) of Generation III the infant mortality was very high; but, on the contrary, every member of Generation II has lived to adult age.

The other cataractous sister of II, 2 (viz., II, 6), has at present only one child (III, 15) believed to be normal. The normals II, 3 and 7, have normal children.

Case 109 (Fig. 51), Kunn [58], (1889), published, from Fuchs's practice, the following case of lamellar cataract in three generations.

Generation I, 1.—Cataract in early life, no details.

Generation II, 1.—Her daughter, operated by Arlt at æt. 6 for lamellar cataract and still sees well. Square ("rickety") skull.

Generation III, 1 to 4.—Issue of II, 1, order of birth not given. Two are normal; the other two, boys of 7 and 5 years (Nos. 1 and 2), had lamellar cataracts which in No. 2 was diagnosed at æt. $1\frac{1}{2}$ years, and showed a threefold layer of opacity; they had no fits, but their bones were rickety and they had "rachitic" teeth. (The youngest boy's teeth would still be the milk set.—E. N.)

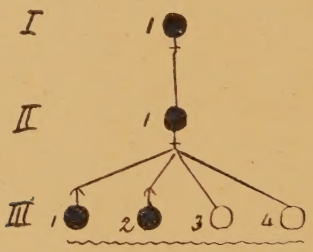


Fig. 51.

Case 110 (Fig. 52).—In 1893 Fromaget [59] published the following case of congenital, probably lamellar, cataract hereditary through five generations. Transmission was continuous throughout, and, except for the first generation, always took place through the mother. The cataract in the children (Generation V) consisted of "alternate opaque and clear layers"; two of the patients (III, 2 and V, 1) had had iridectomy performed in childhood. Probably, therefore, the cataract was lamellar in all the cases. In III, 2, at the date of publication the cataract seems to have been complete, but the patient declined further treatment. Her mother was the youngest of four daughters who had cataract from birth (Generation II); their father and one of his brothers were also reported to have had congenital cataract (Generation I). Of the four in Generation II, three had

gone out of reach and nothing more was known of them; only the mother of Generation III could be traced. III, 2 (Mde. P.), had 14 children, of whom two were born with cataract (IV, 1 and 2), a son and a daughter. The son was unmarried, the daughter (IV, 2) married, and at the time of writing was aged 28 and had had six children (V, 1 to 6); No. 1, aged 11, had undergone iridectomy for her cataracts at the age of 8; No. 4, aged 5; and No. 5, aged 3½, also had double congenital cataract; Nos. 2 and 3 were not affected; and No. 6, who died at the age of 3 weeks, was also believed to be free. No consanguinity of any of the parents.

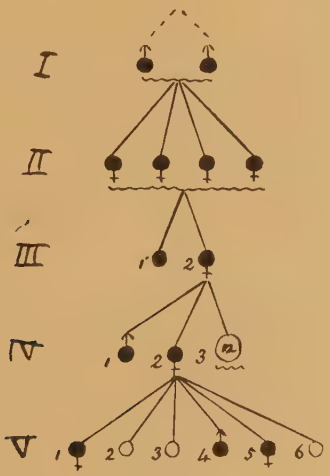


FIG. 52.

CASE 111 (Fig. 53).—Nolte's [57] case (Becker) is as follows:—

Generation I, 1.—Mrs. Becker, cataract formed in both eyes after whooping cough, at the age of 12 both were needled, L. lost by injury some years later. No. 2, her husband, good eyes. Issue, five children, viz.:

Generation II, I.—Christopher. Normal, has four normal children (III, 1).

2. Marie. Cataract, said to be lamellar, not examined.

3. Mathäus. "Lamellar" cataract diagnosed soon after birth. At about the age of 6 optical iridectomy down—in each

eye. When 18 (1879) patient badly developed, severe nystagmus, corneal diameter 10 mm., in each lens a central opacity with projections into the cortex and in R. the cortex is cloudy. R. needled now, and again in 1889. In 1895 R. with +10 D, fingers 3 m., some remains of lens. L. cortex now opaque in coloboma, V. Fingers $1\frac{1}{4}$ m., lens removed, good operative result V. +10 D, fingers 10 m.

4. Elise, normal, has one normal child.

5. Child (sex not stated) with lamellar cataract. Died in early infancy.

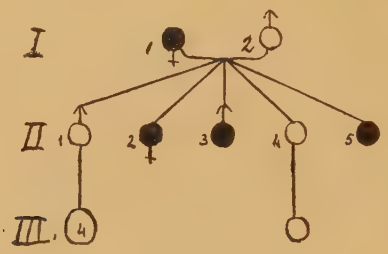


Fig. 53.

II. Case 112 (Fig. 54), Zirm [60] and Bergmeister's case of *Congenital stellate cortical cataract (partly published, partly communicated by Professor Bergmeister)*.

The particulars furnishing the following extensive and exhaustively worked out pedigree were published in part by Zirm, at that time First Assistant at Vienna, in Zehender's Klin-Monatsbl., January, 1892, pp. 5 to 30, and postscript, p. 40; and again, in ignorance of Zirm's paper and with the important addition of Generation VI, by Professor Bergmeister at one of the Vienna medical societies on December 3, 1892. *Case* 47 *in my former paper, erroneously attributed to Ziem, gives part of the same pedigree.* Professor Bergmeister informs me by letter that the whole family (name Löwy) was Jewish, but that as to consanguinity he has no information; nor is consanguinity mentioned by Zirm, in his otherwise full report. The first of the series to be seen was Eugen Löwy, No. 8 of Generation V, a boy of 14 whose case Zirm describes at length as a type of all the

others, illustrating it with two figures. Zirm says that a similar case described by Otto Becker from Arlt's clinic, years before, had since been ascertained to be one of these Löwys.

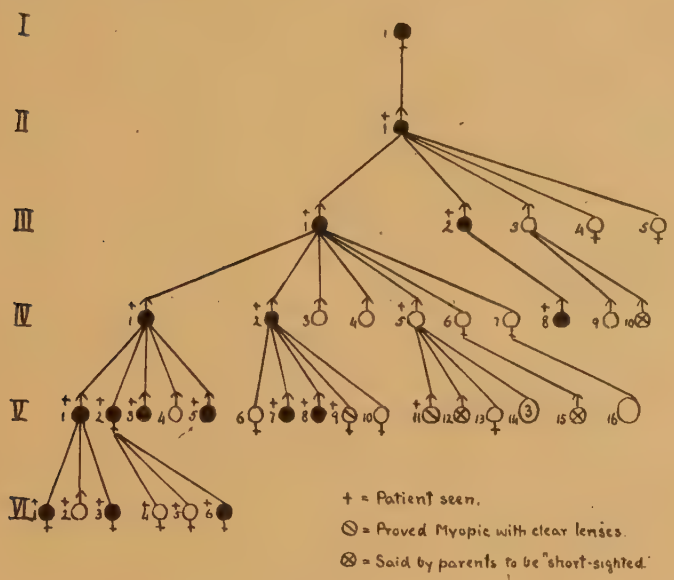


FIG. 54.

Generation I, 1.—Woman became blind, cause unknown.

Generation II.—Son of I, 1. Senile cataract. Had five children (III, 1 to 5). His wife had good eyes.

Generation III, 1.—Moriz L. Both eyes operated for senile cataract. His descendants are shown in Generation IV, 1 to 7, and Generations V and VI.

Generation III, 2.—Samuel L., when æt. 71 found to have stellate cataract. His only child (IV, 8) has the same form of cataract.

Generation III.—3, 4, and 5 all see well. No. 3 has two sons (IV, 9 and 10).

Generation IV.—1 to 7, issue of III, 1. 1, Samuel L., æt. 57 to 58 (1891 and 1892), mixed stellate and senile cataract both eyes, almost complete in L., in R. closely resembling the stellate cataract in V. 8 (below). Strong man with normal bones.

2. Max, 43 to 45, V. defective *from early life*, now stellate cataract with also numerous punctate opacities. My. 1/6 V. corrected = 20/70, fundus badly seen. Bones and teeth normal.

3. Alexander and 4 Adolf, both dead, no details. (The great difference of age between 1 and 2 suggests that Alexander and Adolf really came between Samuel and Max.—E. N.)

5. Leopold, 42. Lenses clear, fundi normal. Both Em., R. full V., L. 20/100 and 16 J. = congenital amblyopia without history of squint.

6 and 7. Daughters, good eyes, married.

8. Moriz, 40. Stellate cataract. No issue.

9 and 10. Sons. One has good eyes, the other said to be "short-sighted."

Generation V.—1 to 5 issue of IV, 1.

1. Jacques, 34 to 35. Stellate cataract, My. 4 D, V. corrected 20/50, unaided 2 J, held very close. Ophth. n. no posterior staphyloma. Teeth n. Health good.

2. Rosa. Stellate cataract. Married.

3. Max, 23. Stellate C.

4. Henri, 21. Normal eyes.

5. Lothar, 16. Stellate C.

Generation V.—6 to 10, issue of IV, 2.

6. Mathilde L. Good sight, "not short-sighted."

7. Isidor, 19 to 20. Stellate C. My. about 4 D. V, corrected 20/50 Ophth. n., no posterior staphyloma. Bones and teeth n.

8. Eugen, 14. Came for glasses in April, 1891; delicately built but healthy, teeth good, no signs of past rickets. *Sight somewhat defective as long as he can remember.* By focal light the anterior cortex of each lens shows five long radial striæ which become enlarged (club-shaped) at peripheral end; at posterior cortex a second stellate figure of three primary spokes dividing into six, all broader, shorter and somewhat denser than the anterior spokes; between the anterior striæ, especially the lower ones, delicate punctiform and linear spots. By transmitted light many finer striæ come into view. All of the opacities stop short of the equator, leaving that part quite clear. Fundi n.; V, My. 4 D, corrected 20/70. Appearances well shown in Zirm's Plate, Figs. 1 and 2.

9. Paula, 11 to 12. Lenses clear; My. R. 1/10, L. 1/18, no note of V.; Fundi n. No posterior staphyloma.

10. Sidonie, sees well, "not short-sighted."

11 to 16. Children of IV, 5, 6, and 7. Of these only No. 11 was examined; he had corneal nebulæ, no cataract, My. 4 D, without posterior staphyloma, V, corrected 20/50 partly with the better (R.) eye.

Nos. 12 and 15 said to be "short-sighted," all the others reported to have good sight.

Generation VI.—1 to 3, issue of V, 1. Seen and described by Bergmeister only.

1. Hilda, L. 8 (December, 1892). Stellate C.
2. Marcel, 5. Normal.
3. Erna, 4. Stellate C.

Generation VI.—4 to 6, issue of V, 2, seen by Bergmeister only.

4. Lina, 9, and 5, Marie, 7; both normal.
6. Friederiecke, 5. Stellate C.

Zirm mentions another isolated case of C. Stellata in a boy (like the Löwys, a Jew) in whom the refraction was H 5 D, and concludes therefrom that in those of the Löwy family who were both cataractous and myopic (*e.g.*, IV, 2, V, 1, 7 and 8 on pedigree) the My. was axial not lenticular. (He might also have cited Case V, 11, where there was My. with clear lenses.—E. N.)

III. *Other Varieties of Congenital Cataract.*

Case 113, Fig. 55. Millikin [55] (Author's Case 3.)—German family. Congenital cataract in two generations, combined with axial myopia.

Generation I, 1.—Mother æt. 44, examined and eyes found normal.

Generation I, 2.—Father æt. 46, both eyes operated for cataract about æt. 40; fundus showed myopic changes. Had all his life had poor sight, but no positive information whether cataracts were congenital.

Generation II, 1 to 7.—Issue of 1. Nos. 1, 2, and 7, good eyes; no note of their refraction.

Nos. 3, 4, 5, and 6, all showed "congenital central opacities of lens varying somewhat in shape and size" with V. from 3/60 to counting fingers. Eyes well formed and patients well grown. All 4 were operated upon with good results. Nos. 4 and 5 had H. only 6 D. and 7 D. respectively after operation, and must therefore have been myopic before.

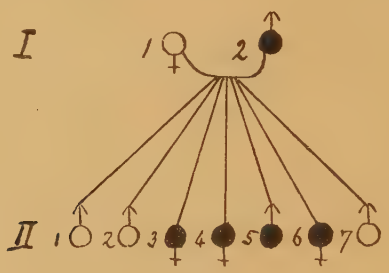


FIG. 55.

CASE 114, Fig. 56. (Millikin gives the following, Case 2.)—Congenital cataract in 5 females, in three generations; lenses small and hard.

Generation I.—A Swedish woman operated for congenital cataract; age at operation not stated. *Generation II.* Her two daughters both operated for double congenital cataract, No. 2 when 6 years of age, No. 1 when young. No. 2 died 6 months after operation. No. 1 grew up and had two daughters (no other children); both were born with double cataract; (III, 1 and 2). III, 1, needled at æt. 9 months and did well; lenses small and hard. III, 2, not operated till æt. 5 years, but did well. All the five cataractous subjects were strong and healthy.

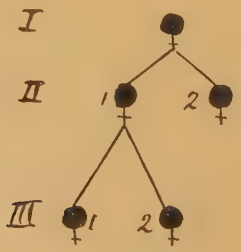


FIG. 56.

Schnabel [56] gives the following two cases of congenital "nuclear" cataract in several siblings, without evidence of inheritance from parents, grandparents, or any other relatives.

CASE 115 (Author's Case 1, Orthaber).—Three siblings aged 8, 6, and 3 years with double "nuclear" cataract.

CASE 116 (Author's Case 2, Lechner).—Three siblings aged 6½ years, 3 years and 8 weeks with double "nuclear" cataract.

CASE 117.—Guiot [61] Année Méd. de Caen, 1890, XV, 264.

A young mother with double congenital cataract which had been operated with poor result. Her first-born child (male) seen at three months of age with "incomplete central" cataract in both eyes.

CASE 118, Fig. 57.—Nolte [57] gives the following example of the occurrence of hereditary (doubtless congenital) cataract, and of other defects, including partial albinism without cataract, in various members of a family named Steitz.

Generation I, 1.—Mrs. Steitz (née Heppel) æt. 47, nuclear and general cataracts, both extracted with success; age at onset not given. Her brother (I, 2) was blind from cataract at æt. 43.

Generation II, 1 to 3.—Seven children of I, 1; of these 5 appear to be normal, but the first-born (1) Christine, 22, has "indications of hare-lip," though otherwise normal; and the 2nd, Maria, 18, has very fair complexion and fundus of eye highly deficient in pigment (the word albinism is not used either here or for the similar cases below, nor is there any note of V.; but Author intimates clearly that he considered the condition abnormal).

Generation II, 4 to 8.—Children of I, 2.

4. Katharina. Posterior polar and zonular cataracts in both eyes.

5. Elizabeth, 23. Congenital deficiency of pigment at fundus. No note of V.; II, 1 D.

6. Jacob, 18.
7. Heinrich, 12. } Both show the same deficiency of ocular pigment as Nos. 2 and 5 above. No note as to V.

8. Son, idiotic and with over-ripe cataracts.

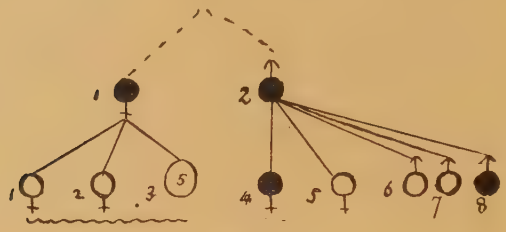


Fig. 57.

Case 119, Fig. 58.—Pisenti [62]. Congenital shrunken cataract, nystagmus and hydrocephalus in 3 of 6 children. Parents first cousins, who themselves inherit mental degeneracy.

Generation I, 1.—Died insane.

Generation II, 1.—Paul, imbecile. Two brothers were epileptic; of his 5 sisters 2 were hysterical, 1 had religious mania, and 2 were tubercular. Paul married II. 2, not related by blood; she had 1 sister (Annie, II. 3), who married an "eccentric" man (3a), and after bearing three children (III. 5 to 7) died at æt. 30 probably of some disease of nervous system.

Generation III.—1 to 4 issue of II, 1 and 2. No. 1 died of tubercle æt. 18; 2 and 3 had religious mania; No. 4 married his maternal first cousin (III, 5), whose two brothers (6 and 7) had

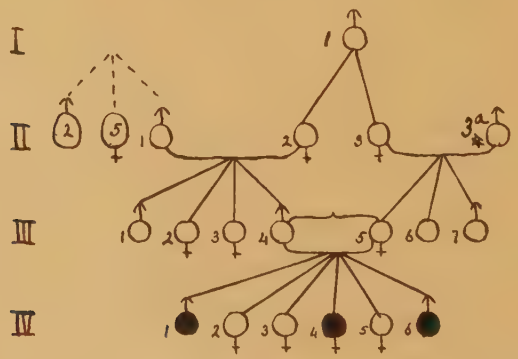


Fig. 58.

weak intellect and alcoholic mania respectively. The cousins, 4 and 5, are not stated to have been unsound, but their children (*Generation IV*, 1 *to* 6) were as follows:—

1. Dead.
4. Living, æt. 4½.
6. Milk teeth carious.

} These three had shrunken congenital cataract and nystagmus, with hydrocephalus.

2 and 3, living and fairly normal; 2 has convergent squint.
5. Died (æt. 3) of tubercular meningitis.

CASE 120.—Congenital cataract, probably complete, running through 4 generations and affecting 15 persons. A. D. Williams, 1880 [63]. Order of birth not stated.

Generation I. ↕ ● Blind from congenital cataract. Had 4 blind children (Generation II), and some not blind (number not stated).

II, 1. ↕ ● Congenital cataract; had 7 children (Generation III), of whom 3 (III, 1, 2, 3) had the same cataract.

„ 2. ↕ ● The same kind of cataract; had 2 children (Generation III, 4, 5) similarly affected.

„ 3. ↕ ● Same cataract. Had 5 children (Generation III), of whom 1 (↕ ● III, 6) and 1 other (III, 7) (sex not stated) affected; 3 unaffected. The cataractous son, III, 6, had 4 children (Generation IV), of whom 3 (IV, 1, 2, 3) were blind from cataract, and inmates of the St. Louis Blind Asylum.

„ 4. ● Fourth cataractous child of I, 1; no particulars.

Postscript to Case 46 *of previous paper, p.* 209 (*Fukala's case*).

Reference to the original paper has since allowed of more precision as to the age of onset of the cataract in several of the patients. In No. 1 (*Generation I*) *it came on at* 40 *years of age, in Nos.* 2 *to* 10 (*Generation II*) *between* 20 *and* 40; *in the three patients indicated by No. II* (*Generation III*) *at* 20, 22, *and* 23 *respectively; and in the first of the three indicated by No.* 13 (*Generation III*), *a woman, the cataract was present at* 30. *The condition was, therefore, præsenile in probably all, with some, but not very marked, "anticipation."*

Postscript.—The proof of the above had been corrected before I saw the paper by Dr. Casey A. Wood on the same subject, giving three new cases (Ophth. Record, vol. xv, p. 142, April, 1906). The cases are :—

1. *Charlton.*—4 generations : I. ♂ blind from cataract. II. Daughter of I, free. III. Daughter of II, cataract. IV. 12 children of III, of whom 10 (5 ♀, 5 ♂) have juvenile cataract ; it is not clear that all these 10 were examined, but in one of them, ♂ æt 33, the cataract is lamellar ; Nos. 10 and 11 of this childship, free, both ♀.

2. *Hussa.*—Cataract beginning in childhood and becoming advanced before old age (in one case at 40) ; 3 generations : I. ♂ cataract. II. 6 children of I, the 1st and 2nd ♀ and 4th ♂ affected, 3rd and 6th ♂ and 5th ♀ free. III. (*a*) 8 children of II, 1, the 1st, 2nd and 3rd ♀ and 5th ♂ affected, 4th, 6th and 7th ♂ and 8th ♀ free. (*b*) 5 children of II, 4, 1st ♂ and 3rd ♀ affected, 2nd ♀, 4th and 5th ♂ free. (*c*) 4 children of II, 6 (herself free), 1st ♂ and 4th ♀ affected, 2nd ♀ and 3rd ♂ free.

3. *Ira Smith.*—Cataract beginning about puberty, but not becoming dense till about 60 ; spontaneous improvement of V in some ; glaucoma in some. 3 generations : I. Both parents free. II. 6 children of I, the 1st ♀ 2nd ♂ and 6th ♀ cataract, 3rd and 5th ♂ and 4th ♀ free. III. (*a*) 7 children of II, 2, 1st and 5th ♂ cataract, Nos. 2, 3, 4, 6 ♀ and 7 ♂ free. (*b*) 4 children of II, 6, 1st ♂ cataract, 2nd and 3rd ♀ and 4th ♂ free.

Case 1 may be compared with my Case 97 in regard to the large proportion affected. Dr. Wood points out that I have omitted to mention some cases in American literature ; two of these (Millikin and A. D. Williams) and a third (Green, of St. Louis, not mentioned by Dr. Casey Wood himself) are given in the present paper ; Hansell's case, which seems important, I knew of, but have been unable to see the original.

List of Authors.

(The numbering is continued from the list at p. 246.)

53. 1890. Green (John). Trans. American Ophth. Soc., vol. v, p. 725.
54. 1891. Hall (G. C.). Indian Medical Record, 1891, p. 194.
55. 1904. Millikin. American Journ. of Ophth., 1904, p. 74.
56. 1891. Schnabel. Ü. Cataracta der Kinder. Wiener Med. Wochenschr., 1891, No. 4.
57. 1896. Nolte (Fritz). Beitrag z. d. Lehre v. d. Erblichkeit v. Augenerkrankungen. Inaug. Diss., Marburg, p. 13 *et seq.*
58. 1889. Kunn. Vererbung d. Schichstaars in einer Familie. Wien. klin. Wochenschr., 1889, No. 3.
59. 1893. Fromaget. Gaz. hebd. d. Sc. Méd. de Bordeaux, 30 Juillet, 1893, p. 368.
60. 1892. Zirm. Klin. Monatsbl. f. A., 1892, p. 5 and p. 40 (January). (Erroneously named *Ziem* as Case 47 in my previous paper.)
Bergmeister. Additional particulars of same family communicated by letter.
61. 1890. Guiot. Année Méd. de Caen, 1890, vol. 15, p. 264.
62. 1900. Pisenti. An. d'Oculist, 123, p. 354, 1900.
63. 1880. Williams, A. D. St. Louis Medical and Surgical Journal, April 5, 1880.

EXTENSIVE CONGENITAL OPACITY OF RETINA IN YELLOW-SPOT REGION OF BOTH EYES. ? OPAQUE NERVE-FIBRES. HIGH MYOPIA ALSO PROBABLY CONGENITAL. CASE UNDER NOTICE 15 YEARS.

By E. Nettleship.

(With Plate I.)

In this case the difficulty is to interpret the ophthalmoscopic appearances; the coloured plate renders any lengthy description unnecessary. In each eye an oval area of the retina extending from the temporal side of the disc up to, and somewhat beyond, the yellow-spot, is opaque and white. The upper and lower borders of the patch and the part of it attached to the disc are fairly well defined and so dense as to entirely hide the choroid, but on the central part of the oval and at its temporal end the opacity is thinner and allows more or less of the choroidal red to shine through; but there was never any clear spot at the fovea centralis. The opacity is finely striated in the direction of the normal nerve-fibres of the region; the retinal vessels covered by the opacity in some places, superficial to it in others; at the temporal end of the affected area the choroid can be dimly seen to be mottled with ill-defined pigment spots between which it appears to be somewhat thinned (yellowish instead of the normal red). At the upper border of the o.d. the opacity disappears insensibly into a well-marked white scleral ring with pigmented border. The appearances were the same in the two eyes, but in the L. whilst the upper border of the opaque area was as dense as in the R. the lower border was thinner and less defined. In all other respects the fundi were perfectly healthy and showed no ordinary myopic changes.

In the first note, taken when the patient was 5 years old,

I compared the opacity to retinal embolism; four years later when she was 9 the drawing was made and my note ends with "the appearances are very similar to opaque nerve fibres." I do not think there had been any alteration between the two dates, but the first examination was less satisfactory than the second.

I saw this girl repeatedly between August, 1886, when she was 5, and January, 1900, and she was seen twice after that date by Mr. Holmes Spicer, who has kindly given me his notes and a sketch of the R. fundus that he made on the last occasion, January, 1902, when the patient was between 20 and 21. The following is a summary, omitting the description of the fundus already given :—

1886. August, æt. 5. Shadow test shows My. about 16 D. with a little As. in each eye; ophthalmoscopic estimation gives My. about 27 D. V. of R. (or better) eye not noted; with L. spells 14 J.

1888. January. Careful ophthalmoscopic note. Milk teeth all still present and good.

1891. May, æt. 9. Drawings of both fundi made by Miss Stone. (Plate I represents the R. eye.) Refraction by retinoscopy; R. My. 20 D.; L. My. 19 D.; no As. in either. R. −18 D. sees 3/36, L. −15 D. 3/60; no note of near vision. Ordered spectacles for distance R. − 16 D.; L. − 13 D.

1891. December, V. both eyes together with the above spectacles 3/60 to 3/36. Unaided reads 1 J. very close, and about 6 J. at 3 to 4 inches. Reads a good deal and makes no complaint.

1892. November. Reads much, and even small print, always without glasses. Chooses −18 or 20 D. with each eye, and with such lens sees 4/60 with both together. Thin and pale; teeth have been troublesome lately.

1895. January, æt. 13. V. both together with −20 4/60. Colour vision (wool test) normal. Choroid at and near the temporal end of the affected area in each is perhaps more patchy than when drawings were made.

1898. January, reads 2 J. with R. Mr. Donald Gunn finds some vacuoles and other small opacities in each lens, more

in L., and slight opacities in vitreous. Details at y.s. in R. seen with −25 D., and in L. with −28 D. (I have no earlier note of careful examination of the lenses, and some opacities may have been present from the first.) Has just passed the matriculation examination of the University of London, and is ambitious to teach mathematics. Question of removal of L. lens considered.

1899. January. Lenticular opacities somewhat increased; they take the form of dotted radii at posterior cortex and are most pronounced at nasal side; opacities in vitreous not increased; appearances of choroidal atrophy at y.s. rather more marked.

1900. January. All as last time; no increase of lenticular opacities.

1902. January, æt. 20 to 21. Mr. Holmes Spicer made a sketch of R. fundus and described the retinal opacity as having all the ophthalmoscopic characters of opaque nerve-fibres; through the thinnest parts he saw appearances of a large area of superficial choroidal atrophy; there was also a patch of choroidal atrophy above the o.d. away from the opaque retina and evidence of sclerosis of some of the choroidal vessels. The opacities in the lenses may have increased, for they now somewhat obscured the fundus, and with the R. (better) eye she read 4 J. at 3 inches instead of 2 or 1 J.; L. still read 12 J. as at the first examination, and V. of both together with −20 D. was still 4/60, as it was with same lens when she was 9 or 10 years old (1891 and 1892).

Subsequently she went as a teacher to Germany. She was independent in her habits, disliking assistance, and this led to her death by an accident when walking alone in the autumn of 1905, at the age of 25.

If the retinal opacity in this case was not due to ordinary congenital opacity of the nerve-fibre layer, can any other explanation be given? One knows of no other congenital condition producing such appearances, and the tolerably good vision in the better (R.) eye proved that the deeper layers of the retina were in good condition. On the other hand, the opacity occupied the macular region, which is supposed never to be subject to this peculiarity; it was more exactly

symmetrical and more nearly equal in quantity in the two eyes than in most cases of opaque nerve-fibres; some choroidal change was certainly present beneath the opacity when she was only 9 years old, and although this had become more marked by the time she grew up it was still almost confined to the area underlying the altered retina and was not associated with ordinary myopic changes. It is difficult to suppose that the opaque area represented an abrupt and steep-sided, macular staphyloma; but such a condition cannot be quite excluded, because no comparative estimation of the degree of the myopia at the y.s. and elsewhere was ever made. Although, as already stated, the comparatively good vision of the R. eye disproved any very serious affection either of the percipient or the conducting elements of the retina, the appearance of more or less choroidal change quite early in life in both eyes, together with the much higher amblyopia of the L., in which nevertheless the retinal opacity was somewhat less, may point to the whole process having started in the choroid in fœtal life and caused not only the protrusion indicated by the myopia but secondary changes in the retina. It must be admitted, however, that this explanation is purely hypothetical. The lenticular opacities had little or no share in causing the defect of sight.

Family history. The patient was the youngest of a childship of eight, was born at full time when her mother was 39 or 40, was suckled, and never in her life had an important illness. There were in all 10 pregnancies in 16 years; the third and one other ended in miscarriage, the other 8 gave living children of whom all except the subject of this paper are still alive (1906), healthy and with normal sight (except anisometropia in the second, see below). There was an interval of 3 years between No. 7 and No. 8 (the patient). From the history it is probable that the mother had heart disease for some years before the patient's birth. The second child, a boy 11 years her senior, was examined at Moorfields when he was eighteen; he had slight

H. in the right eye, My. 2 D. in the L., V. of each being full with correction. The patient's father and mother were not myopic, but two of the father's sisters and their mother were said to have been so. The father is living and well (1906); the mother, who had cardiac disease, died about 1896, aged 54.

Bale & Danielsson, Ltd. lith.

EHRLICH'S THEORY OF IMMUNITY IN ITS RELATIONSHIP TO OPHTHALMOLOGY.

By J. Herbert Parsons.

The investigation of the processes which underlie the various forms of immunity to the action of toxic agents in the body has led to far-reaching results which have an important bearing upon nutrition, not only in its pathological, but also in its physiological manifestations. The researches of Metchnikoff and his colleagues at the Pasteur Institute and of Ehrlich and his followers have thrown a flood of light upon cell-life, and though the subject is one of great complexity it can no longer be ignored in dealing with the problems of physiology and pathology. It is only recently that the influence of the theory of immunity has made itself felt in the domain of ophthalmology, almost entirely owing to the researches of Römer, himself a pupil of Ehrlich. In order that the relation of immunity to ophthalmic problems may be comprehensible, it is necessary to give a brief account of the evolution of the theory, more particularly as enunciated by Ehrlich.

The fundamental peculiarity of living cells is the elective affinity which they exhibit for certain substances which are useful for their nutrition, the substances varying with the type of cell. Chemical and physical processes have hitherto failed to give a satisfactory explanation of this peculiarity. It is well known that synthetic processes occur in the metabolism of the cell. Substances which are available for the nutrition of the cell must be such as are capable of being assimilated and synthetically bound up in the cell. In order that this may occur chemical groups must exist in the cell and in the food stuff which possess strong affinity for each other. These chemically active groups in the living

protoplasm, which have a maximal affinity for definite groups in the food substances and which serve to anchor the latter to the cell, are called by Ehrlich *side-chains* of the protoplasm or *receptors*. According to the side-chain theory the specific nutrition of individual types of cells is due to the possession by the living protoplasm of atom complexes which are capable of linking on certain other atom complexes, thus adding them to the protoplasmic molecule.

The side-chain theory is founded upon the analogy of the benzene ring, in which, by the linking on of other chemical groups, the character of the substance is entirely changed, though the benzene nucleus remains intact. Ehrlich first expounded the theory in 1888, in a book upon the need of the organism for oxygen.

Antitoxins.—Ehrlich's fundamental proposition found its earliest and most important application in explaining the production of antitoxins. Antitoxins had already been prepared by methods which were almost entirely empirical; the *rationale* of their formation was merely a matter of conjecture. Their origin, and the enormous quantities which it was possible to obtain in small volumes of serum, had not yet been satisfactorily explained. It was natural to suppose that the toxin was directly transformed into antitoxin, but this failed wholly to account for the quantities produced. Their most striking feature was their specific activity. Diphtheria antitoxin protected only against diphtheria, tetanus antitoxin only against tetanus. This characteristic especially pointed to the direct transformation of toxin into antitoxin, a view which was held by Buchner and Metchnikoff. Facts which militated against this theory rapidly accumulated. Some of the more striking may be mentioned. Thus, one part of toxin might give rise to 100,000 parts of antitoxin (Knorr). An animal might be deprived of nearly the whole of its blood by bleeding, but after a short interval the antitoxin content of the newly formed blood had reached its former level (Salomonsen and Madsen, Roux and Vaillard). Moreover, antitoxins are

present in the blood of quite normal animals, *e.g.*, diphtheria antitoxin and tetanolysin antitoxin in horses, staphylotoxin antitoxin in man, etc. Everything pointed to the fact that antitoxin production was a function of the living organism.

The investigations were first put upon a sound basis by Ehrlich's experiments with ricin and abrin. These poisons when administered to animals lead to the production of specific antitoxins, and Ehrlich succeeded in obtaining accurate quantitative estimates of the relationship between the dose of poison and the degree of immunity. From his experiments Ehrlich was led to apply his side-chain theory to the explanation of the problem. The bacterial poisons are substances which nearly approximate to proteids in their chemical constitution. Individual poisons possess atomic groupings which correspond with those of certain food substances. When such a poison is introduced into the body the possibility arises of the toxin entering into direct chemical relationship with the protoplasm of suitable cell-types. If the toxin possesses groups which are identical with those of the food stuff, it will become chemically anchored to the protoplasm. Ehrlich went a step farther, enunciating the essential axiom of the theory of immunity. Directly the toxin is anchored to a receptor the latter can no longer fulfil its physiological function. If the function of the cell is not so severely affected as to cause the death of the cell, its protoplasm possesses the capacity of replacing the disabled side-chain. Not only so, over-compensation occurs, and more receptors are formed than are essential to the metabolic functions of the cell. This is especially the case when the stimulus is repeated, as is effected in immunisation by renewed doses of toxin. Finally, a time is reached when so many receptors are produced that they form an encumbrance to the cell. They are then cast off into the blood. Since they still retain the atom-complex which enables them to anchor the toxin, they now act as antitoxin. In the words of v. Behring, "the same substance in the living body, which, when present in the cell, is the

postulate and condition of poisoning, becomes the cause of cure when circulating in the blood stream."

The next problem to be solved was the nature of the action of the toxin upon the antitoxin. If a certain dose of diphtheria toxin in bouillon is injected into a guinea-pig, the animal dies with characteristic symptoms. If previously a sufficient dose of antitoxin has been injected, the animal remains healthy. The same result occurs if the toxin and antitoxin are mixed before injection. No change is seen to occur in the serum when the mixture is made. An antitoxic serum is apparently exactly like a normal serum; indeed, v. Behring has shown that the antitoxin is absolutely harmless.

The first proof that the action of the antitoxin upon the toxin is a direct chemical combination, was shown in Ehrlich's experiments with ricin. More striking perhaps were the later experiments of Martin and Cherry with diphtheria. If a diphtheria serum is passed through a gelatinised Pasteur-Chamberland filter it loses its antitoxic character. Diphtheria toxin, on the other hand, passes through such a filter with little loss of toxicity. If therefore a mixture of the two be passed through the filter, we may expect the filtrate to be toxic if the mixture is merely a mixture of the toxin with the antitoxin, whereas if the two have entered into chemical combination they may be expected to pass through intact. Martin and Cherry showed that the filtrate was absolutely innocuous.

The same investigators have proved by another method that chemical combination occurs. If Calmette's antitoxin to snake poison is warmed for 10 minutes it ceases to be antitoxic; the same treatment has no effect upon the poison itself. Mixtures of the toxin and antitoxin were kept for 30 minutes at 20° C. After warming to 68° C. the mixture was found to be quite innocuous.

These and other such experiments prove also that the combination of the toxin with the antitoxin is independent of the organism, since it occurs equally well *in vitro*.

Further, as in all chemical combinations, the law of multiples obtains. If 1 c.c. of antitoxic serum suffices to neutralise 100 lethal doses of poison, 3 c.c. will render 300 such doses inactive (v. Behring, Knorr, Ehrlich, Cobbet and Kanthack, Römer).

These researches negative the Roux-Buchner theory that the antitoxin has no direct action on the toxin but acts upon the cells. Römer has confirmed the results in the actual presence of living cells by using the conjunctival sac as a test-tube. If a drop of jequirity solution is instilled into the conjunctival sac, the abrin contained in it causes the development of a croupous conjunctivitis after a short incubation period. If on the other hand a mixture of abrin solution and antitoxin, in such proportion that the toxin is neutralised and anchored to the antitoxin, is instilled, the eye remains as quiet as if physiological salt solution had been used. If the slightest excess of toxin is present inflammation results. Römer has elaborated the principle so as to afford a new method of quantitatively estimating the interaction of abrin and antiabrin. It may be pointed out that an animal cannot be immunised by such a neutral toxin-antitoxin mixture, since all the toxin is rendered ineffective, not only for causing an inflammatory response, but also for stimulating the over-production of receptors which is the basis of immunity. The same mixture is neutral to any animal, whether injected into a mouse, instilled into the eye of a rabbit, or injected into the circulation of the highly susceptible guinea-pig.

From the clinical standpoint antitoxin has a double *rôle*—prophylactic and curative. The prophylactic effect is comprehensible on Ehrlich's theory from the circulation of large quantities of unsatisfied receptors in the blood circulation. The curative effect is less easily understood. According to Metchnikoff the process is not brought to an end by the mere combination of toxin and antitoxin. The leucocytes are supposed to play an important part in making the organism proof against the toxin. The union of toxin with

antitoxin simply raises the value of the toxin as a food material for the leucocytes. According to Ehrlich, however the curative effect of the antitoxin is due to the ability of the antitoxin to dissociate the toxin from combinations which it has already made with the tissues of the body. As an example the curative effect of tetanus antitoxin may be cited. Dönitz has shown that tetanotoxin is immediately taken up from the blood by the tissues, so that when a large amount is injected the lethal dose is fixed in four to eight minutes. The anchored poison is dissociated from the tissues by the antitetanus serum, is forthwith neutralised and rendered innocuous. The dissociation is the more difficult the longer the interval between poisoning and the introduction of the serum. Although the toxin is fixed by the cells in a few minutes, yet cure may be effected after 30 minutes by the administration of five to ten times the neutralising dose of antitoxin. After a longer interval the strongest dose of antitoxin fails to save the animal.

Römer's experiments with abrin are of special interest to the ophthalmologist in this connection. By the administration of antiabrin the inflammation produced by jequirity can be controlled. Not only is any free abrin which may be present neutralised, but that already combined with the tissues is set free and neutralised. Even more striking is the fact that the application need not be local to the conjunctival sac, for subcutaneous, intravenous, or intraperitoneal injection effects the same result. Here it is obvious that the antitoxin circulating in the blood and lymph has the capacity of attacking the toxin fixed by the cells.

Careful consideration of the mode of action of organic toxins affords suggestive inferences as to the structure of the toxin molecule. Three features stand out prominently, viz., the specific activity of the toxin, its capacity to give rise to antitoxin, and the existence of an incubation period. The last fact emphasises the difference of toxins from most chemical poisons. For example, even if tetanotoxin is injected directly into the brain, the cells of which show

a special avidity for it, yet a definite latent period occurs before poisoning sets in (Roux and Borrel). To explain this peculiarity, Ehrlich conjectures that every toxin molecule contains two different chemical groups, a haptophore group and a toxophore group. The *haptophore group* subserves the combination of the toxin molecule with the cell, which for its part possesses a complemental unsatisfied group, viz., the receptor. The *toxophore group* is the nocuous element, which cannot exert its influence until linked on to the cell through the mediation of the haptophore group. On the side-chain theory the two groups are otherwise essentially independent.

The effect of the simpler chemical poisons, *e.g.*, alkaloids, upon the cell is rapid and short-lived. The effect of organic toxins is slow and prolonged. They induce metabolic changes which modify the whole life-history of the cell; hence the analogy which Ehrlich delineated between their activity and cellular nutrition. Indeed, the analogy is very striking, especially when viewed in the light of Emil Fischer's experiments on ferment action. The activity of ferments is conditioned by the possession of a definite atomic grouping, which shows a specific avidity for a complemental grouping in the substance attacked. Only such substances as possess the complemental group are subservient to the activity of the ferment, just as a lock can only be opened by a certain key. Further analogies are found in the physiological activity of definite atomic groups in synthetic hypnotics, anæsthetics, etc., *e.g.*, the ethyl group is prepotent in hypnotics, the benzoic acid group in anæsthetics.

As regards the toxophore group, its enormous toxicity is noticeable: 0·0000004 gramme of the tetanus poison is the lethal dose for a mouse. The next most notable feature is its lability; slight influences suffice to attenuate its activity. Most striking in this respect is the fact that the attenuated virus does not lose its capacity for producing antitoxin. Hence Ehrlich hypothecated a second, stable, haptophore

group in the toxin molecule, and it is this group which not only conditions the anchoring of the toxin to the cell, and so activates its toxicity, but also subserves the production of the antitoxin. This is shown by the fact that toxins whose haptophore groups are satisfied by antitoxin are no longer suitable for immunisation; they have lost their capacity for inducing the formation of antitoxin.

The experimental proof of the existence in the toxin molecule of two different groups was given by Morgenroth. He made use of the discovery by Courmont and Doyon (1892), that the frog, although insusceptible to tetanus at the ordinary temperature, became affected if kept at a raised temperature. This might be due to one of two causes: either the toxin did not become anchored to the nerve cells at the lower temperature, or, though anchored, the toxic element was not capable of acting at this temperature. That the latter was the true explanation is shown by the fact that the longer the animal was kept in the cold after injection of the toxin, the more antitoxin it was necessary to inject in order to protect it from tetanus on warming. Moreover, the same fact was confirmed by observation of the incubation period. Thus, the usual incubation time after raising the temperature is two to three days. Morgenroth kept frogs for 24 hours at 32° C., and then replaced them in the ice chest for days or weeks; on again warming them tetanus supervened after an incubation period which was never shorter than the normal by more than 24 hours. In other words, the cold interval was simply intercalated; on warming, incubation went on exactly from the point at which it had been stopped. Hibernation has exactly the same effect (Billinger, Dönitz). The presence of two groups in the toxin molecule has also been shown by Neisser and Wechsberg's researches on staphylolysin, the poison formed by the staphylococcus which has the power of dissolving the hæmoglobin out of red corpuscles.

The facts and theoretical considerations which have hitherto been discussed apply to those toxins which are

secreted by bacterial organisms and cast off into the surrounding medium, *e.g.*, diphtheria, tetanus, etc. There are other pathogenic organisms which do not excrete the whole of their poisons but keep them locked up in their own tissues, *e.g.*, typhoid, cholera, plague, etc. Here the action of antitoxins is different and more complicated, but it is probable that they act as specific bactericidal agents. Two early hypotheses as to the cause of immunity in these diseases may be quickly dismissed. It was considered probable that the organism during the first attack used up all the available nutrient material, which it was supposed must be of a specific nature. Another view was founded on the fact that bacteria produce excretion products which have an inhibitory effect upon their own growth. As was proved by Flügge and his pupils, however, there is no evidence that any such products are retained indefinitely in the body. Finally, Metchnikoff attributes to the leucocytes the *rôle* of destroying the bacteria by ingestion.

In 1896 an important observation was made by Pfeiffer. If a subminimal lethal dose of typhoid bacilli, or a dose of bacilli mixed with serum from an immunised animal, is injected into the peritoneal cavity of a guinea-pig, and specimens of the peritoneal exudates are examined under suitable conditions, it will be found that in a few seconds after injection the bacilli have lost their motility. Moreover they rapidly undergo changes in appearance. The bacteria become swollen and break up into granules, which soon dissolve entirely in the fluid, so that the number of organisms quickly diminishes. According to the Ehrlich theory this phenomenon is due to the presence of antitoxins in the fluid, though this is denied by Metchnikoff.

The analogy of the breaking up of bacteria to the well-known breaking up of red corpuscles under certain circumstances, led to the latter phenomenon being carefully studied from this standpoint. There can be no doubt that the least exceptionable evidence in favour of Ehrlich's theory is to be

found in the beautiful experiments which have been made on hæmolysis.

Hæmolysins.—It has long been known that the serum of many animals has the power of dissolving the hæmoglobin out of the red corpuscles of the blood of other animals, especially if the latter belong to a quite distinct species. The subject was investigated by Landois, and is responsible for the abandoning of blood transfusion. In 1898 Belfanti and Carbone showed that the serum of horses became much more toxic to rabbits if rabbits' blood had been previously injected into the horses. Bordet attributed this to the formation of specific hæmolytic substances. He injected repeatedly 3 to 5 c.c. of defibrinated rabbit's blood into the peritoneal cavity of a guinea-pig; the serum of this animal rapidly dissolved the hæmoglobin out of the red corpuscles of rabbit's blood *in vitro*, though normal guinea-pig's serum has little or no such power. Confirmatory experiments by Landsteiner and v. Dungern and others proved the extraordinary specificity of the reaction. It may be stated, as a general rule, that if the red corpuscles of one species are injected subcutaneously, intraperitoneally, or intravenously into another species the serum of the latter—"immunised"—animal becomes toxic to the erythrocytes of the former animal. It is clear that differences in osmotic pressure fail to explain the phenomenon, since a fraction of a milligram of serum cannot alter the tonicity of the fluid, as may indeed be proved by adding it to an isotonic saline solution. According to Ehrlich, hæmolysis is the sign of protoplasmic death in the stroma of the erythrocytes. It is usual to speak of the escape of hæmoglobin as solution of the blood cells, though the stroma is not destroyed.

Further experiments showed that the analogy between antitoxins and hæmolysins extended to their chemical behaviour. Bordet found that if fresh hæmolytic serum was warmed to 55° C. and kept at this temperature for half an hour it became inactive. If a small quantity of normal guinea-pig's serum, which is also hæmolytically inactive,

was added to this inactive serum it again became hæmolytic to rabbit's blood. Hæmolysis is therefore due to the presence of two substances, one of which is present preformed in the animal's serum, whilst the other is formed by the process of immunisation. Bordet called the thermostable element substance sensibilisatrice; it has since received many other names—preparator (Gruber), helping body (Buchner), copula (P. Müller), desmon (London), philocytase or fixator (Metchnikoff), immune body or between body (Ehrlich and Morgenroth). Ehrlich has finally settled on the name *amboceptor*, which has been generally adopted. Bordet thought that the thermolabile substance was identical with Buchner's alexin, which is a substance in serum acting upon bacteria and foreign blood corpuscles like an enzyme. It has since been called addiment or finally *complement* by Ehrlich, and cytase by Metchnikoff.

It has already been mentioned that hæmolysins are specific. Thus, rabbit's serum immunised for guinea-pig's blood is only active to guinea-pig's erythrocytes; it will not dissolve sheep's erythrocytes. From this fact Ehrlich concluded that either the amboceptor or the complement possessed a specific affinity for some atom-complex in the red cell. Ehrlich and Morgenroth proved it in the following manner:—A goat was immunised by injection of sheep's blood. The serum was warmed at 55° C., so that the complement was destroyed. One cubic centimetre of this inactive serum was added to 4 c.c. of 5-per-cent. sheep's blood; the mixture was kept at 40° C. for 15 minutes and then centrifuged. To the clear fluid 0·2 c.c. of normal sheep's blood and 0·8 c.c. of normal goat's blood were added, and the mixture was kept at 37° C. for two hours; not a trace of solution occurred. The sediment from the centrifuging was then washed in 4 c.c. of 0·85-per-cent. salt solution, and 0·8 c.c. of normal goat's serum was added; in two hours there was complete solution. The experiment proves that the amboceptor was absorbed by the red

corpuscles; only on the addition of a small quantity of normal serum containing the complement was solution obtained. It was not, however, a simple absorption, for if so, other red corpuscles might be expected to serve the purpose equally well. This was not the case; hence, there is a definite specific chemical combination. The corpuscles can be repeatedly washed with physiological saline solution without causing any dissociation of the amboceptor from the cells. Quantitative experiments show that the amount of amboceptor anchored varies in different cases.

Ehrlich concludes from these experiments that the amboceptor possesses a haptophore group by means of which it becomes anchored to a receptor in the cell.

Corresponding experiments with the complement showed that this is not taken up by the corpuscles. Investigations carried out at different temperatures showed that the haptophore group of the amboceptor united with the receptor of the erythrocytes in the cold, whereas its affinity for the complement is less, and is only manifested at a higher temperature. It must, therefore, possess another haptophore group which is complementophile. Since the union of the complement can only be carried out by means of the cytophile and complementophile groups of the thermostable substance, this was suitably called the amboceptor. It finds its analogy in organic chemistry in diazobenzaldehyde. The analogy between a hæmolysin and a toxin scarcely requires to be pointed out; the haptophore group of the toxin is represented by the amboceptor, the toxophore by the complement. Bacterial hæmolysins have been described for pyocyaneus (Bulloch and Hunter), for streptococci (Basredka and Marmorek), for diphtheria (Lubenau), for typhoid (E. and P. Levy), etc. Snake poisons also contain hæmolysins (Stephens and Myers, Flexner and Noguchi).

It is unnecessary here to enter into the much-disputed question of the site of formation of the antitoxic and hæmolytic constituents. The specific nature of the ambo-

ceptor and the multiplicity of complements may be mentioned. The similarity of the complement to a ferment is emphasised in Metchnikoff's name—cytase. There is a striking parallel in the *rôle* of enterokinase in digestive processes and that of the complement in hæmolysins. It is not improbable that this fact may point the way to some general law of wide applicability, which will evolve order out of the chaos of these and similar difficult problems of physiology.

Neither is it necessary here more than to mention that hæmolysins may, under suitable conditions, give rise to antihæmolysins. Isohæmolysins, and autohæmolysins, or bodies which cause solution of the hæmoglobin from the cells of the animals of the same species or of the same animal, have also been described; they, too, give rise to antibodies. Their importance can scarcely be exaggerated, but little is yet known about them.

The facts of hæmolysis have been utilised by Römer in attacking two problems of ophthalmology—one therapeutic, the other pathological. In the former hæmolysins have been injected into the vitreous in cases of intraocular hæmorrhage with a view to assisting in breaking up the red cells and promoting absorption. In some cases the results have been favourable, but in others necrosis of the tissues has shown that the method is not without danger (Elschnig).

By the aid of hæmolysins Römer has brought forward the most delicate evidence against the ciliary nerve theory of sympathetic ophthalmia. According to this theory the irritation of the ciliary nerves in the exciting eye causes a sort of symmetrical irritation of the ciliary nerves of the other eye, so that the way is prepared for the sympathetic inflammation. If such irritation occur it is to be expected that it will manifest itself by increased hyperæmia of the ciliary body, and this will be followed by the transudation of a more highly albuminous lymph than normal. Wessely investigated the problem by estimating the amount of proteid in the aqueous of each eye after one had been

irritated severely. He found no increase in the second eye, and his results have been confirmed by Tornabene. Such experiments to decide so delicate a point are too crude to be of much value, since the error of experiment is probably fully as large as any alteration which might be reasonably anticipated. The hæmolysin test is far more delicate. Römer first confirmed the observation of earlier investigators that no hæmolysins are present in the aqueous of immunised animals, *e.g.*, if a rabbit is immunised against ox corpuscles by the injection of 15 to 20 c.c. of ox blood into the peritoneal cavity, the rabbit's aqueous will not dissolve ox corpuscles. If, however, the aqueous is drawn off a second time after an interval of three-quarters of an hour it is powerfully hæmolytic. The delicacy of the test is shown by the fact that a milligram of the second aqueous will dissolve 50 or 60 million red corpuscles. Now, intense irritation of one eye does not cause the slightest trace of hæmolysin to appear in the normal aqueous of the other eye, whilst in every iritis and iridocyclitis, no matter how slight, hæmolysins are at once found in the aqueous of the first eye.

It was possible that the complement might already be present in the normal aqueous, whilst perhaps only the immunising body, the amboceptor, which in serum is chiefly attached to the globulins, entered with the regenerated aqueous. An exactly titrated hæmolytic serum was heated to 60° C: hæmolysis only occurred if 0·01 active normal serum, containing the complement, was added to 0·0008 c.c. of this, which contained the amboceptor. It was found that even 0·2 c.c. of first-drawn aqueous added to 0·0008 c.c. of the inactive immunised serum failed to cause hæmolysis. The complement was therefore not already present; it only appeared when the aqueous was regenerated. It was similarly proved absent from the first aqueous of the immunised animal. In an analogous manner it was also proved that the amboceptor was not already present in the first aqueous of the immunised animal. After puncture the

complement appeared in the aqueous of the normal animal, and also the amboceptor in the immunised animal.

Römer further showed that the complement was present in the aqueous one hour after subconjunctival injection of 4 per cent. salt solution.

One eye was irritated by various means—a chip of copper in the anterior chamber, injection of dead typhoid bacilli or staphylococci into the vitreous, etc. In every case the first aqueous was hæmolytic in the injured eye but not in the other. The same result followed chronic intraocular inflammation caused by the injection of a non-pathogenic culture of bacillus subtilis. Further, although the second aqueous of the uninjured eye naturally contained hæmolysins, these disappeared in 24 hours. The experiments were also confirmed on monkeys immunised with ox-blood.

Bacteriolysins.—Reference has already been made to Pfeiffer's experiment (*vide* page 47). It is not my intention to enter into details as to the mechanism of bacteriolysis, nor into the cognate question of bacterial immunity. It will be remembered that it is a matter here of organisms such as typhoid, cholera, plague, pneumonia, etc., which exert their main influence, not by virtue of excreted toxins as do the tetanus and diphtheria bacilli, but by noxious properties contained in themselves. The subject is of enormous importance in the whole range of medicine, but chiefly from the prophylactic and therapeutic points of view.

It seems certain that the injection of dead cultures of the type of organism under consideration produces a definite reaction whereby the leucocytes are stimulated to increased bacteriolytic activity. The chemical stimuli which produce this result have been called *opsonins* by Wright.

It may be mentioned in passing that Römer has instituted a campaign in this field also. It has already been pointed out that the majority of cases of ulcus serpens are due to the pneumococcus. Statistical researches show that more than half the accidental wounds of the eye

eventuate in ulcus serpens (Römer). Römer has shown that the eye can be protected against pneumococci by immunisation. As a prophylactic method the results are perfect in rabbits; as a curative method they are successful if the remedy is applied early. The immune serum is best obtained from rabbits, even when used for man. Römer maintains that early immunisation by antipneumococcic serum in man protects against the development of ulcus serpens, and that even progressive hypopyon ulcers can be brought under control.

Agglutinins, Precipitins.—Agglutinins, which have an ætiological importance in general medicine, and precipitins, which bid fair to assume a preponderant *rôle* in forensic medicine, have not hitherto given evidence of much importance in ophthalmology. It is sufficient to mention here that, while receptors of the first order, such as serve to anchor toxins, ferments, and other cell secretions, possess only one haptophore group, those of the second order, which serve to bring about agglutination and precipitation, possess a haptophore group and a zymophore group. Agglutinins and precipitins pass readily into the aqueous; hence they are doubtless innocuous and are probably valuable as food material.

Cytotoxins.—The discovery of substances having a specific destructive influence upon red corpuscles naturally led to investigation as to the existence of specific poisons for other types of cells.

v. Dungern injected ciliated epithelium from the trachea of the ox into the peritoneal cavity of the guinea-pig. He found that the cells retained movement in their cilia for two days; in a week or so all the cells have disappeared. A fresh dose of epithelium was injected 10—12 days later. In 18 hours all the cells had disappeared. Hence the animal had acquired a distinctly increased power of destroying the cells. Further research brought out the interesting fact that the serum of animals immunised against ciliated epithelium of the ox was hæmolytic to ox-red corpuscles.

Hence ciliated epithelium and erythrocytes must possess the same or nearly allied receptors. Even the injection of milk into a rabbit produced a serum which contained cytotoxins to ciliated epithelium and hæmolysins to ox-blood.

An immense amount of work has been done on the same lines with spermatozoa by Metchnikoff and his pupils and others (Landsteiner, Moxter). The spermotoxic serum is also hæmolytic. On the other hand, Metchnikoff has shown that a hæmolytic serum produced by injection of blood is not spermotoxic, whilst the spermatozoa in a serum produced by simultaneous injection of spermatozoa and blood possesses the capacity of anchoring both the hæmolytic and the spermotoxic amboceptors.

Delezenne and Centanni have produced neurotoxins by the injection of brain substance. Many other cytotoxins have been investigated, *e.g.*, liver (Delezenne, Schütze, Deutsch, Hulot and Ramond), kidney (Bierry, Lindemann, and others), placenta—synzytiotoxin (Ascoli and others), ovary (Ceconi and Robecchi), suprarenal (Bigart and Bernard, Sartirana), pancreas (Surmont, Carnot, Garnier), stomach (Théohari and Babès, C. Bolton), pituitary body (Collina), thyroid (Gontscharnkoff, Mankowski, Sartirana).

More interesting to ophthalmologists are the conjectures of Römer as to the cause of senile cataract deduced from the side-chain theory. He compares the lens to a red corpuscle, each having a surrounding membrane which impedes the diffusion outwards of important constituents. When the hæmoglobin has passed out of the erythrocyte the cell is dead; so, too, cataract is the expression of the protoplasmic death of the lens fibres. Previous observations in hæmolysis have shown that isohæmolysins can be formed, *e.g.*, in the goat (Ehrlich and Morgenroth); autohæmolysins, on the other hand, are only formed under pathological circumstances. If autocytotoxins occur it might be expected that they would be a sign of senile change, for atrophy and degeneration of tissues are the common features of old age.

Now it is necessary, if lentotoxins occur, that they should be able to reach the lens, or rather that the lens should be protected from them under normal circumstances. Hence the importance of knowing the behaviour of the secretory apparatus of the eye with regard to such bodies. It may be pointed out here that the essential feature of cytotoxin activity is its fixation by the cell; this has nothing to do with osmotic conditions, but as soon as the cell is poisoned osmotic processes will have free play.

It has already been mentioned that neither constituent of hæmolysin, neither amboceptor nor complement, is present in the aqueous either of the normal or the immunised animal. Receptors of the second order—viz., agglutinins (Metchnikoff, Wessely, Römer) and precipitins (Römer), pass freely through into the aqueous. These, however, do not act as cytotoxins, for the latter are always receptors of the third order, *i.e.*, amboceptors with two haptophore groups one cytophile, the other complementophile. Teleological considerations would lead one to suppose that substances of this type are not suited for nutrition of the lens and vitreous.

Römer has succeeded in showing that there are receptors of the second order in the lens. *i.e.*, such as possess a haptophore and a zymophore group, and may be distinguished by their agglutinative properties. He has further shown that there are receptors of the first order present, *i.e.*, such as possess a haptophore group which is capable of combining with substances of the type of toxins, ferments, and other cell secretions. He has also shown that there are complementophile receptors in the lens, and that these exhibit definite specificity. The experiments are too complicated for minute consideration here; they must be studied in the original communication. They tend, however, to support the theory that senile cataract is a result of the specific activity of lentotoxins.

Römer has recently investigated the question of retinal cytotoxins. Cytotoxins as a cause for cyclitis is a thesis

which has not yet been investigated, but would appear *a priori* to be specially likely to give affirmative results. These curiously insidious cases give every sign of toxic activity. In many cases a septic focus can be found in some part of the body, especially in the mouth—pyorrhea alveolaris, etc. Here doubtless the cyclitis is the result of a bacterial toxæmia. In other cases in which no cause can be discovered it is not improbable that the essential factor is a specific cyclotoxin.

In my opinion, however, the work which has been done on cytotoxins in general is the weakest part of the structure which has been built on the basis of the side-chain theory. It is impossible at present to attempt to correlate the isolated facts which have already accumulated. It may be expected that further research, and especially the valuable criticisms and investigations of the Metchnikoff school, will eventuate in the discovery of some general principle underlying these complex problems.

Bibliography.

Römer. Die Ehrlichsche Seitenkettentheorie u. ihre Bedeutung f. d. med. Wissenschaften. Wien, 1904. (Bibliography.)

——— Arch. f. Ophth., vol. lii, 1, 1901. (Jequirity.)

——— Arch. f. Ophth., vol. liv, 1, 1902. (Ulcus serpens.)

——— Arch. f. Ophth., vol. lv, 2, 1903. (Sympathetic Ophthalmia.)

——— Arch. f. Ophth., vol. lx, 2, 1905. (Senile Cataract.)

Hess and Römer. Arch. f. Augenheilkunde, vol. liv, 1, 1906. (Retina.)

Elschnig. Zeitschr. f. Augenheilkunde, vol. xi, 1905.

Metchnikoff. Immunity in Infective Diseases, translated by Binnie. London, 1905.

AN ANALYSIS OF A SERIES OF CONSECUTIVE CONJUNCTIVITIS CASES SEEN IN ABERDEEN.

By C. H. Usher and Henry Fraser, Aberdeen.

As no record exists of the micro-organisms which cause conjunctivitis in this part of the country, we were led to observe clinically and bacteriologically the cases on which this article is based, and in order to arrive at the relative frequency of such organisms, a series of consecutive cases was taken. Throughout the inquiry attention was paid to the question of how far, by means of clinical characters, a conjunctivitis caused by a certain micro-organism may be distinguished from that produced by other micro-organisms. In May, 1904, preliminary observations were commenced with a view to determine the methods which would best suit our requirements. Films from the discharge of various cases were made and examined. The growth of the different micro-organisms was the next consideration. A study of the literature showed that the diplobacillus of Morax and Axenfeld did not give rise to much difficulty in its cultivation. The Koch-Week's bacillus, on the contrary, appeared to require very favourable conditions for its growth. Axenfeld* states that for the growth of the diplobacillus blood-serum agar or medium mixed with human fluids should be employed. Agar mixed with one-third hydrocele or ovarian fluid is excellent. Ascitic fluid may also be employed. Morax† states that for the growth of the diplobacillus we must employ agar mixed with serum in accordance with Wertheim's method. Morax employed

* Centralblatt für Bacteriologie, January, 1897. Über die chronische diplobacillen conjunctivitis.

† Note sur un Diplobacille Pathogene pour le conj. humaine. Annales de l'institute Pasteur, 1896, p. 337.

ascitic fluid for this purpose. Morax and Bach state that the best medium is a mixture of human serum and agar.* We decided to commence with ascitic agar. The ascitic fluid was collected under aseptic precautions, a sterilised trochar and cannula with rubber tube attachment being used to withdraw the fluid. The first portions of the fluid were allowed to run off and then sterilised filter flasks were charged with the fluid. Both openings were closed in the usual manner with sterilised cotton wool. It may be remarked of fluids collected in this manner that they have remained aseptic for seven or eight months, notwithstanding that their amounts were constantly diminished by frequent use. A 2-per-cent. agar was employed, standardised to a reaction of + 10 phenolphthalein, which was placed in test-tubes and sterilised thereafter in the autoclave. At first the method recommended by Morax was employed. The agar was liquefied and cooled to 60° C., one-third part of serum was then added to each test-tube and carefully mixed. The tubes were sloped, and, when the mixture was solid, they were placed in the incubator for 48 hours to test their sterility. This process of cooling to 60° C. was soon found to be unnecessary. The tubes were placed in a water bath and the agar liquefied, the wool plug was removed from the lateral tube in the flasks employed for collecting the fluids, the lateral tube and the parts adjacent were then sterilised by means of a Bunsen flame, and the tubes of liquefied agar had then added to them the requisite amount of fluid. The contents of the tubes were carefully mixed, sloped and allowed to solidify. After preparation of a batch of tubes, the lateral tube was carefully wiped free of fluid by wool and thereafter replugged with cotton wool, and the lateral tube so plugged was sterilised by means of a Bunsen flame. This method has been employed for over 18 months, upwards of a dozen various fluids being used and more than 1,500 tubes of media prepared, without

* Quoted from Weichselbaum and Muller: Über der Koch-Weekschen Bacillen der acuten conjunctivitis. Arch. f. Ophthalmologie, 1898, p. 108.

in a single instance the fluids or media being contaminated. The ascitic agar furnished growths of the diplobacillus of Morax and the gonococcus, but it did not yield evident growths of the Koch-Week's bacillus. It was then decided to try ovarian fluid. On substituting this for the ascitic fluid during an epidemic of Koch-Week's conjunctivitis, beautiful colonies of the bacillus were obtained. Some of these were pure cultures which were subsequently sub-cultured through as many as 40 generations. Comparative cultures of the Koch-Week's bacillus so obtained on ascitic and ovarian agar did not show an appreciable difference in the appearance of their colonies, yet the growth on ovarian agar was more profuse, and on the whole much more satisfactory.

When sufficient experience had been gained in the recognition of various micro-organisms met with in the conjunctival sac and of the clinical conditions associated with these, a series of 100 cases, for the most part consecutive, was investigated. For this series a chart was devised, by the aid of which a clinical diagnosis of the organism present was made. In certain cases it was confirmed by the bacteriological examination, in others it was not. An analysis of the cases was made, with a view to determine the value of each of the clinical characters as an aid in forming a diagnosis, and so increase, if possible, the accuracy of a clinical diagnosis in a subsequent series. Some features seemed to be associated with certain specific micro-organisms. The reliability of these was again repeatedly tested on other cases before the commencement of an examination of a further series of consecutive conjunctivitis cases.

During the year 1905, all cases of conjunctivitis coming to the Aberdeen Royal Infirmary and Dispensary were examined. In order to bring the clinical characters of each case into line, for purposes of comparison, the following schedule was filled up in each instance at the time of examination:—

Date . Number of case .
Sex . Infirmary .
Age . Dispensary .
Aberdeen or .
Complaint—Gritty or similar feeling. Heavy lids.
Difficulty in reading. Gumminess of lids.
Rainbows. Other complaints.
Interval since onset of attack .
Previous attacks .
Others with sore eyes (1) in same house ; (2) elsewhere .
Colour of conjunctiva (*a*) palpebral ; (*b*) ocular .
Amount of discharge (1) none or very slight; (2) moderate; (3) profuse.
Character of discharge (1) purulent; (2) muco-purulent.
Follicles enlarged .
Conjunctival hæmorrhages .
Chemosis .
Membrane on conjunctiva .
Swelling of lids .
Preauricular gland enlarged .
Eye affected R. ; L. .
Corneal ulcer ; phlyctenules ; impetigo ; nasal discharge ; ear discharge .
Clinical diagnosis of organism present .
Film .
Culture .

Notes of "Angular Conjunctivitis" were not recorded until July 1, 1905. Certain cases of conjunctivitis were not included in the series, namely, those obviously due to injury and those in which lachrymal obstruction occurred. A difficulty presented itself as regards cases in which phlyctenules were present. Those only were included in which the conjunctival congestion was not limited to the neighbourhood of the phlyctenule.

The micro-organisms which we attempted to clinically forecast as being present in the conjunctival sac, were Koch-Week's bacillus, the diplobacillus of Morax and Axenfeld, the gonococcus, the tubercle bacillus and the diphtheria bacillus. When it was believed that none of these forms could be demonstrated by a bacteriological examination, a diagnosis of "other forms" was made. This term is employed for the sake of brevity throughout this article.

Technique Employed in the Consecutive Series Examined in 1905.

It was originally intended to take two films and one culture from each case, one film to be stained in the usual manner by Löeffler's methylene blue. Should a doubt arise as to the presence of certain organisms, the other film would be stained by the method of Gram. The scarcity of discharge in many of the cases rendered this triple procedure impossible, and at times it had to be decided whether to take a single film or only a culture. Hence, as a routine practice, a single film and a culture were taken.

Films.—The material from the conjunctival sac was removed by means of a sterilised platinum wire and smeared over a glass slide. It was dried by exposure to the air, fixed by heat, stained by means of Löeffler's methylene blue, and examined microscopically.

Cultures.—During the preliminary observations 2-per-cent. agar was employed and the body fluids were added in the proportion of one to three. Later the amount of fluid added was increased, but it was found that media so prepared were not sufficiently firm to retain a sufficiently level surface when exposed to the heat of the incubator. 2·5-per-cent. agar was thereafter employed, mixed with equal parts of the body fluids. This method was retained throughout the consecutive series. In all, nine body fluids were used for the cases in this series. Some of these were early abandoned, others proved so satisfactory that they were employed until they were exhausted. The striking difference in the relative value of various fluids led latterly to a rough investigation as to the amount of albumin in them, and to evidence of the presence of blood; the early fluids were not tested. The media and fluids employed in the inquiry are designated as follows:—

A. Ovarian fluid obtained in 1904.

B. Ovarian fluid obtained on March 11, 1905. This fluid tested by Esbach's albuminometer showed 7 per cent. of albumin present. A portion of the fluid heated with ammonia and ammonium sulphide gave the spectrum of hæmochromogen.

C. Ovarian fluid obtained on April 29, 1905 (not tested).

D. Ascitic fluid obtained on April 29, 1905, contained 4 per cent. of albumin and did not yield the hæmochromogen spectrum.

E. Parovarian fluid obtained on July 29, 1905, contained 0·15 per cent. of albumin; spectrum of hæmochromogen not obtained.

F. Ovarian fluid obtained on October 7, 1905, contained 7·5 per cent. of albumin; spectrum of hæmochromogen observed.

G. Ovarian fluid got on November 25, 1905, contained 5 per cent. of albumin; spectrum of hæmochromogen observed.

H. Ovarian fluid got on December 15, 1905, contained 5 per cent. of albumin; hæmochromogen present.

I. Hydrocele fluid got on September 7, 1905; 5½ per cent. of albumin and no hæmochromogen.

The number of conjunctivitis cases in the consecutive series examined during 1905 was 820. The total number of all eye cases was 3,527. Conjunctivitis, therefore, formed 23·24 per cent of the cases. In v. Michel's Jahresbericht, statistics, extending from 1885 to 1895, from various clinics in different countries, embracing 599,595 cases of eye disease, showed that the most frequent eye disease was that affecting the conjunctiva. It amounted to 28·5 per cent. Cohn, in a collection of 297,326 cases, found that conjunctival diseases were 30 per cent.

Koch-Week's Conjunctivitis.

There were 310 bacteriologically proved cases of this form in the series of 820 cases of conjunctivitis.

Out of the 820 cases there were selected :—

(1) All cases clinically diagnosed as due to Koch-Week's bacillus.

(2) All cases bacteriologically proved to have Koch-Week's bacillus present.

These were then grouped as follows :—

1. Cases clinically diagnosed as due to Koch-Week's bacillus and confirmed bacteriologically. There were 268 cases. Of these, 242 were clinically diagnosed as due to Koch-Week's bacillus and bacteriologically confirmed, hereafter referred to as Group A. Twenty-six cases, clinically diagnosed as due to Koch-Week's bacillus, were proved bacteriologically to have in association both Koch-Week's bacillus and the diplobacillus ; hereafter referred to as Group B.

2. Cases diagnosed clinically as due to Koch-Week's-bacillus but not confirmed as such bacteriologically. In this group were 78 cases, hereafter referred to as Group C.

3. Cases wrongly diagnosed—30 as "other forms," 12 as diplobacillus—which were shown bacteriologically to be due to Koch-Week's bacillus. In this group were 42 cases, hereafter referred to as Group D.

In all, 388 cases were thus analysed. As far as possible the age, history and objective signs of the cases in each of these groups are given in tabular form. The various items noted in the schedules are given seriatim.

Age Incidence.

Age.	Group.				
	A.	B.	C.	D.	A + D.
Under 1 year ...	17	1	3	4	21
1—4 years	53	8	10	3	56
5—13 years	144	13	40	14	158
Above 13 years ...	28	4	25	21	49
Total cases ...	242	26	78	42	284

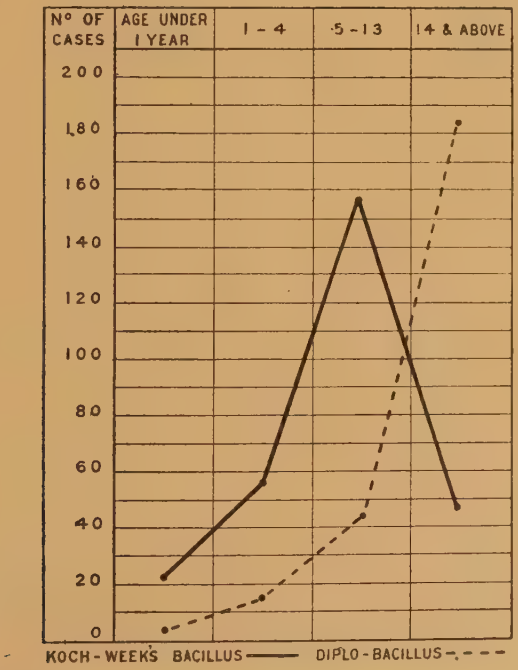


Table to show, at different age periods, the relative prevalence of conjunctivitis, proved bacteriologically to be due to—

(1) Koch-Week's bacillus } (exclusive of the cases in which both these
(2) Diplobacillus } organisms were found associated.)

Interval since Onset of the Attack.

In Group A (242 cases), presumably the more typical cases, it was found that the average length of the period during which symptoms had been present was 6·8 days. In 42 the interval was not more than 2 days. In 77 there was an interval of from 3 to 4 days. Sixty-seven patients came for treatment at the end of 7 days; 25 on the 14th day, and only 10 came after a longer period, of whom 5 came at 21 days; one, an infant of ten months, was said to have had symptoms of conjunctivitis for four months. In Group B (26 cases) 25 came for treatment on an average after an interval of 5·9 days, 3 of these after symptoms had been present for 14 days; all the others came within one week. The 26th case, the only one clinically diagnosed as containing both Koch-Week's bacillus and the diplobacillus, came after an interval of 21 days. Of 30 cases under Group D recorded clinically as due to "other forms," but which were shown to contain Koch-Week's bacillus, 24 came within a week. One said that symptoms had been present for one year, and another for two years. The remainder came at intervals varying from 14 days to three months. The suggested explanation of the long duration of the symptoms in some of these cases is that the diplobacillus was present as well as Koch-Week's bacillus, and in all likelihood was responsible for symptoms prior to the more recent infection by Koch-Week's bacillus. In Group C (78 cases) 58 came after an interval of not longer than one week.

An attempt was made to determine the duration of this form of conjunctivitis by consulting the case papers. These showed that the vast majority of the cases did not return. The same is true for the diplobacillary cases.

Previous Attacks.

In Group A were 25 cases: 20 of these were under 14 years of age; one, a child of 11 months, was said to have

attended hospital for three months after birth on account of eye disease. We are aware that the previous attacks may have been due to other conditions, as seems likely in the 11 months' child just noted, but that a second attack of Kock-Week's conjunctivitis may occur in the same individual, was proved in the case of two boys. The bacillus was obtained in each case during an attack of conjunctivitis in 1904, and again during a second attack about 18 months later, in 1906.

Group B, no cases. This might favour the view that Koch-Week's bacillus was the primary cause of the infection; recurrences are less common in cases due to the Koch-Week's bacillus than in those due to the diplo-bacillus.

Group C, 17 cases. Five of these would still be regarded as due to Koch-Week's conjunctivitis (*vide infra*).

Group D, 8 cases.

There was, therefore, a history of previous attacks in 33 of 310 cases of Koch-Week's conjunctivitis.

Others Affected with the same Symptoms.

	Group.				
	A.	B.	C.	D.	A + D.
In same house ...	131	16	35	15	146
Elsewhere	58	5	10	3	61

Certain cases gave a history of others affected both in the same house and elsewhere.

In Group A, in 167 cases, there is a history of other persons being affected with similar symptoms. In 131 instances others that were affected lived with either the patient's family or with other families in the same tenement.

In 58 instances other affected persons did not live in the

same house, but some attended the same school. Three-fourths of the cases in this group came as patients to the dispensary, where, generally speaking, a poorer class is seen than at the hospital. Their conditions and habits would favour the spread of an infectious disease.

Group B. In 19 cases it was reported that there were persons affected similarly; in 16 instances the affection being in the same house, in 5 instances elsewhere.

Group C. In 40 cases other individuals were known to be affected; in 35 the affection was in the same house as our patient, in 10 instances it was elsewhere.

As evidence of the infectious nature of Koch-Week's conjunctivitis, may be mentioned the occurrence of several small epidemics which came under our notice during the course of this investigation. In one of these an outbreak occurred in a certain street from which a number of typical Koch-Week's cases were obtained. Three of the cases were members of the same family, others were from adjoining houses. Seven of the cases, representing five different families, from three adjoining tenement houses, were examined. All were Koch-Week's cases. In September 1904, an opportunity arose for investigating an outbreak occurring in an industrial school in Aberdeen. At this institution there are about 130 boys, aged from five to sixteen. At the time of our first visit 12 boys were affected with Koch-Week's conjunctivitis, their ages varying from eight to fourteen years. The specific micro-organism was obtained in each case. Two other boys with the same form of conjunctivitis were examined later. Some cases had occurred previous to our visit. At the end of May, 1904, the first case was observed. On June 20 there were three more, by June 23 four others occurred; by the 30th four more were added, by July 12 there were six new cases. In August, seven new cases occurred. In September nine new cases, 34 in all, or about one-fourth of the inmates in the institution, had been affected. The children used towels in common. The individuals affected were isolated until cured. Notwith-

standing that the condition as regards use of towels, etc., had not been altered, no further case had been reported from September, 1904, until January, 1906. On January 30, 1906, six boys were affected. The attack was mild in each case. There were none with conjunctival hæmorrhages. The Koch-Week's bacillus was found in every case. Three of them had been previously affected in 1904, and at that time in two of these we had found the Koch-Week's bacillus. Recurrences at short intervals have been noted by Morax and Petit and also by L. Müller.* The latter observer described one case in which the interval was several months. Previous epidemics have occurred at this institution, but there is no record of any bacteriological examination.

(1) In May, 1894, 13 boys were affected with ophthalmia.

(2) May and June, 1897, 17 were affected with ophthalmia.

(3) October, 1899, to May, 1900, from 70 to 80 boys were affected.

As regards the relative frequency of Koch-Week's conjunctivitis in town and country, see p. 488. None of the cases in this series came from rural districts.

* Quoted from Kolle u. Wassermann.

Increased Redness of Conjunctiva.

	Group.				
	A.	B.	C.	D.	A + D.
Ocular and palpebral ...	225	22	67	30	255
Palpebral only	17*	4†	11‡	12§	29
Total cases ...	242	26	78	42	284

Of the 310 cases in which Kock-Week's bacillus was shown to be present, 33 had only the palpebral conjunctiva affected. One-third of these (11 in 33) occurred in infants. A moderate amount of discharge was present in three of the 11 cases; in the remaining eight, this was scanty.

Amount of Conjunctival Discharge.

	Group.				
	A.	B.	C.	D.	A + D.
Scanty	65	8	47	29	94
Moderate	158	18	29	13	171
Profuse	19	0	2	0	19
Total cases ...	242	26	78	42	284

* The interval since onset of symptoms in six of these did not exceed seven days, in two it was 14 days, in one it was 21, and in another it was 30 days. Seven occurred during infancy; one of these was said to have had symptoms of conjunctivitis present for four months.

† Of these, one was an infant with symptoms present for one day. Two were in children of three and four years, with symptoms present for seven and 14 days respectively. One was in a woman of 35, with symptoms for eight days.

‡ Ten of these came after symptoms had been present for a week or less, and one after 14 days. In no case was the age less than three or over 25 years.

§ Of these 12, three were in infants. One was in a patient aged 74, Case 421, in which both the diplobacillus and Koch-Week's bacillus were found; one in a patient aged 49, and another was aged 34. In none of the remaining cases did the age exceed 24.

Did the small amount of discharge occur in cases which came at an early or at a late stage of the disease? Of the 65 cases with scanty discharge, in Group A, 43 came within four days of the onset of symptoms, 10 on the 14th day, or later. Of the 29 cases with scanty discharge in Group D, 10 came within four days of the onset of the symptoms, 13 on the 14th day, or later. This gives 94 cases of proved Week's conjunctivitis with scanty discharge, of which 53 occurred within four days of the onset of symptoms, and 23 on the 14th day, or later, *i.e.*, 76 cases occurred within four days or later than 13 days, *i.e.*, 80·85 per cent.

Of the 158 cases with a moderate amount of discharge, in Group A, 70 came within four days of the onset of symptoms; 23 on the 14th day or later. Of the 13 cases with a moderate quantity of discharge, in Group D, 7 came on the 4th day or earlier, 5 on the 14th day or later. On adding together the cases with moderate discharge, in Groups A and D, there are 171 cases of proved Koch-Week's conjunctivitis, of which 77 came within four days of the onset of symptoms and 28 on the 14th day or later, *i.e.*, 105 occurred within four days or later than 13 days, *i.e.*, 61·40 per cent.

Of the 19 cases with profuse discharge in Group A, in 10 symptoms had been present for four days or less, and in two for two weeks or longer.

In Group B, of the eight cases with scanty discharge, two had had symptoms for four days, and in two symptoms had been present for 14 days. Of the 18 cases with moderate discharge, in nine symptoms had been present for four days or less, and in three cases for 14 days.

In Group C, of the 47 cases with scanty discharge, 20 came at an interval not exceeding four days after the onset of the symptoms; six at an interval of two weeks or longer. Of the 29 cases with moderate discharge, six came after an interval of four or fewer days, and 11 cases after 14 days. One with profuse discharge came on the 3rd day, the other on the 7th day.

The Discharge was almost invariably of a muco-purulent character and requires no further comment.

Presence of Enlarged Conjunctival Follicles.

Group A—35,* B—6, C—9, D—8.†

Presence of Conjunctival Hæmorrhage.

Group A—57, B—3, C—13, D—1.

Chemosis.

In Group A chemosis is noted twice; in none of the other three groups was it met with.

Membrane on the conjunctiva was present in four of the cases in Group A.

Presence of Swelling of Lids.

Group A—210, B—22, C—63, D—23.

Presence of Enlarged Preauricular Gland.

Group A—84, B—7, C—32, D—6.

In infants an enlarged preauricular gland has not been observed.

Proportion of Uniocular to Symmetrical Cases.

	Group.			
	A.	B.	C.	D.
Uniocular	21‡	1§	15‖	10¶
Symmetrical...	221	25	63	32

* Thirty-one were in children. † Seven were in children.

‡ Only three of these presented themselves for examination later than the 4th day after the onset of symptoms, one on the 5th day, and two on the 7th day.

§ Symptoms had been present for only one day.

‖ Of these, six came after the 4th day from the onset of the symptoms, one on the 5th day, and five on the 7th day.

¶ In three of these, symptoms had been present for longer than four days. One, a child of seven, had complained for 21 days; another case, aged 34, had symptoms for 30 days; and the third case, a child of three months, for 90 days.

Presence of Corneal Ulcers, etc.

	Group.			
	A.	B.	C.	D.
Corneal ulcers	1	0	2	2
Impetigo	3	1	1	1
Phlyctenules	35	3	6	2
Nasal discharge	16	1	2	0
Aural discharge	1	0	0	0

Phlyctenules were noted in 53 of the 820 cases of conjunctivitis in the series. In 36 of these the staphylococcus was present. In five of the 53 cases Koch-Week's bacillus only was found; in 31 of the 53 cases Koch-Week's bacillus was found in association with one or more of the following micro-organisms: staphylococcus pyogenes aureus and albus, xerosis bacillus and streptococcus pyogenes.

In four of the 53 cases Koch-Week's bacillus and diplobacillus were found together. In two of the 53 cases diplobacilli only were found. In one diplobacillus associated with staphylococcus pyogenes albus and xerosis bacillus. In nine staphylococcus pyogenes aureus and albus or xerosis bacillus, one or more, were found. In one, pneumococcus was found with staphylococcus pyogenes albus.

Clinical Diagnosis.

Subjective symptoms are of but little assistance in distinguishing Koch-Week's conjunctivitis from that caused by other micro-organisms. In three-fourths of the 820 cases of conjunctivitis examined, the complaint made was of a gritty or similar feeling in the eyes, or of gumminess of the lids in the morning. Usually both of these symptoms were present. In the 310 cases where Koch-Week's bacillus has been proved to be present, only 28 times was any other

complaint made, such as difficulty in reading, the appearance of rainbows, etc.

The schedules of the 78 cases in which Koch-Week s bacillus was diagnosed but not found, have been reconsidered, since the facts brought out in the series of 820 cases have been tabulated, and there is reason to believe, from their clinical features, that thirty-two of them were caused by Koch-Week's bacillus, which organism was not obtained because—

(1) The amount of discharge was scanty.

(2) A film only may have been taken.

(3) A culture only may have been taken. When a film and culture are both taken, our experience has shown us that the organism may be absent in one and yet present in the other. It may be that the available discharge was used up for the first specimen, but we are unable to state whether the positive preparation was taken first.

(4) The culture media may have been unsatisfactory.

(5) The interval between the inoculation of the medium with the conjunctival discharge and the placing of the same in the incubator may have been too long. Unavoidable delay sometimes occurred. Squares of linen (5 mm.) soaked in the discharge, placed in sterilised Petri's dishes and exposed to room temperature, yielded cultures of Koch-Week's bacillus after two hours, but not after four. Weichselbaum* and Müller found that particles of secretion placed in a dried Petri dish did not yield cultures after $6\frac{1}{2}$ hours. Hofmann† found after exposing the discharge for three hours in dry Petri's dishes that the bacilli died.

In eight cases in which the pneumococcus was demonstrated, there were no clinical characters which would serve to differentiate them from a conjunctivitis caused by the Koch-Week's bacillus. In ten cases a clinical diagnosis would be a mere hazard. Twenty-five cases should now have

* Archiv f. Ophthalmologie, vol. xlvii, 1899, S. 103, quoted from Kolle u. Wassermann (Handbuch der pathogenen Mikro-org.).

† Zeitschrift f. Hygiene, vol. xxxiii, 1900, S. 109, quoted from Kolle u. Wassermann (Handbuch der pathogenen Mikro-org.).

been diagnosed differently; thus in case No. 3 a patient, age 73, the age alone makes the presence of Koch-Week's bacillus most unlikely, as, in the series, no case of conjunctivitis due to this bacillus has been met with in patients over 50 years of age, with the exception of a single case in which it was present with the diplobacillus. For the same reason Case 53, a patient aged 64, and Case 57, a patient aged 67, would not likely be due to Koch-Week's bacillus.

In the next three examples the history of *previous attacks* would favour the view that the micro-organism present was the diplobacillus.

Case 45, a child of six years, whose conjunctivitis was due to the diplobacillus, is one that would be difficult to distinguish from a Koch-Week's conjunctivitis. One week after the onset of symptoms there was a moderate amount of muco-purulent discharge, both palpebral and ocular conjunctivæ were congested and the lids swollen—signs which, in conjunction with the age, are suggestive of Koch-Week's conjunctivitis. On the other hand, the history of previous attacks would rather favour the view that the conjunctivitis was due to the diplobacillus.

Case 127 should have been recognised as due to the diplobacillus. A male, aged 13, interval since onset of symptoms five days, previous attacks, ocular conjunctiva not congested, scanty discharge, lids swollen and both eyes affected.

Similarly, Case 196, a female, aged 8, interval since onset of symptoms one week, previous attacks, others affected elsewhere, palpebral conjunctiva congested, but the ocular conjunctiva unaffected, moderate amount of muco-purulent discharge, lids swollen and both eyes affected. The diplobacillus was found.

Significance of the Uniocular Character of Conjunctivitis.

Case 134 has but one point which would throw doubt on a diagnosis of the Koch-Week's bacillus, namely, that after one week the affection was still uniocular. In 274 cases of proved Koch-Week's conjunctivitis 32 were uniocular; of these, 26 had had symptoms present for a period of not longer than four days.

Case 134, a female, aged 4, interval since onset of symptoms one week; others affected in the same house; both ocular and palpebral conjunctiva congested; moderate amount of muco-purulent discharge; conjunctival hæmorrhages; lids swollen, and one eye only affected. Film: cocci. Culture: staph. alb.

Cases of Koch-Week's conjunctivitis with only the palpebral conjunctiva affected (33 cases) may present difficulty in diagnosis.

Case 731, a male, aged one, brought after 14 days with the ocular conjunctiva unaffected, a moderate amount of muco-purulent discharge and both lids swollen; was diagnosed as a case of "other forms," but Koch-Week's bacillus was found present.

Cases to illustrate how an accurate diagnosis is impossible when the symptoms are obscured by treatment.

Case 212, a female, aged 27, who came after an interval of 4 weeks, with palpebral and ocular conjunctiva congested and a moderate amount of muco-purulent discharge, enlarged follicles; conjunctival hæmorrhages and both eyes affected. She had been using "golden ointment." In this case Koch-Week's bacillus was diagnosed, but staphylococcus pyogenes albus only was found.

Case 734, a male, aged 30, who had been using yellow ointment. Koch-Week's bacillus was found in the culture. Symptoms had been present for two days. Gumminess of lids; previous attacks; others affected; scanty discharge; swelling of lids; symmetrical. Clinical diagnosis: "other forms."

Conjunctivitis in a child where both palpebral and ocular conjunctiva is congested, the discharge is scanty, and no characteristic symptoms of either Koch-Week's or diplobacillary conjunctivitis are present may be due either to the diplobacillus or to Koch-Week's bacillus. Thus—

Case 23, a child aged 10, with palpebral and ocular conjunctiva congested, scanty discharge and no hæmorrhages or

other characteristic symptoms, diagnosed as Koch-Week's conjunctivitis, proved to be so.

Case 596, a child of 12, with similar symptoms, diagnosed as a case of Koch-Week's conjunctivitis; the diplobacillus was found in film and culture.

The two following cases are given as examples in which Koch-Week's bacillus may have been overlooked.

Case 717, a male child, aged 12, who came after an interval of three days with a history of others being affected in the same house, palpebral and ocular conjunctiva congested, discharge very scanty, lids swollen, and only one eye affected. Cases of conjunctivitis in children (palpebral and ocular conjunctiva congested) with only scanty discharge and where no pathogenic organism is found, are more likely to be due to Koch-Week's bacillus than to the diplobacillus, because (1) Koch-Week's bacillus is more common at this age than the diplobacillus. (2) Koch-Week's bacillus is more easily overlooked.

Case 128, a female, aged 17, who came after an interval of five days with palpebral and ocular conjunctiva congested, a moderate amount of muco-purulent discharge, lids swollen, and both eyes affected; is probably one in which Koch-Week's bacillus was overlooked. The diagnosis was Koch-Week's bacillus; film showed diplobacillus; no organisms were found in the culture; the medium was not satisfactory, and it is quite likely that when the conspicuous diplobacillus was found in the film the search was discontinued. In the 820 cases the Koch-Week's bacillus was shown to be associated with the diplobacillus 36 times. Axenfeld states that this mixed infection, according to general experience, is infrequent.

Of the 32 cases diagnosed as due to "other forms" and bacteriologically proved to contain Koch-Week's bacillus, the same diagnosis would still be made in 18 of them. In 12 a different diagnosis would be given, and in two a diagnosis would only be a guess.

The next four cases were all believed at the clinical examination to have been caused by Koch-Week's bacillus, but for reasons assigned it seemed unlikely that the bacillus

could be demonstrated; in consequence "other forms" were diagnosed.

Case 70, a male, aged two, with symptoms for two weeks, was complicated by the use of yellow ointment. Diagnosis, "other forms." Film and culture—Koch-Week's bacillus.

Case 13, a child, aged 11 weeks, with symptoms present for one day; discharge scanty; others affected elsewhere; previous attacks; uniocular; illustrates what we have from time to time met with, namely, cases which we felt were caused by Koch-Week's bacillus, but where, owing to the scanty discharge and the short duration of symptoms, it was thought unlikely that the bacillus would be obtained, hence the diagnosis of "other forms" in this instance. Koch-Week's bacillus was present.

Case 77, a female, aged 5, also had slight symptoms. Koch-Week's bacillus was found in the film, but not in the culture, which illustrates also the importance of taking both a film and a culture.

Case 730, which was one in which Koch-Week's bacillus was found in the culture but not in the film.

Cases which illustrate the unreliability of history in some instances.

Case 199, a child aged three months, in whom symptoms were said to have been present since birth.

Case 282, a child aged six years, where symptoms had been present for two months. In both of these Koch-Week's bacillus was present.

Case 644, a female age 13, with symptoms said to have been present for longer than a year, a history of previous attacks, no others affected, ocular conjunctiva not congested, scanty muco-purulent discharge, lids swollen and both eyes affected. Koch-Week's bacillus was found.

It is improbable that the symptoms in these cases caused by a conjunctivitis due to Koch-Week's bacillus had lasted for such a long period; for of the 274 proved cases of Koch-Week's conjunctivitis, only six in all gave a longer history than one month.

The clinical diagnosis of Koch-Week's conjunctivitis cannot be based upon one or two symptoms alone, but must depend upon a consideration of several features, namely, the age, history—previous attacks, interval since onset of attack, etc.—and objective symptoms. In a considerable proportion of the cases no doubt can attach itself to the diagnosis, as in these three typical examples :—

Case 700, female, aged 12, living in town, sore eyes and lids gummed in the morning for three davs ; no previous attack ; others affected in the same house ; palpebral and ocular conjunctiva congested ; moderate quantity of muco-purulent discharge ; enlarged follicles ; conjunctival hæmorrhages ; swelling of lids ; preauricular gland enlarged ; symmetrical. Diagnosis : Koch-Week's bacillus. Film and culture gave Koch-Week's bacillus.

Case 445, a male, aged six, living in town, with sore eyes and gumminess of lids for three days ; no previous attack ; others affected in the same house and elsewhere ; palpebral and ocular conjunctiva affected ; moderate quantity of muco-purulent discharge ; conjunctival hæmorrhages ; swelling of lids ; preauricular gland enlarged ; symmetrical ; phlyctenules. Diagnosis : Koch-Week's bacillus. Film and culture showed Koch-Week's bacillus.

Case 704, a female, aged seven, living in town, with sore eyes and gumminess of lids for seven days ; no previous attacks ; others affected in the same house ; palpebral and ocular conjunctiva affected ; moderate quantity of muco-purulent discharge ; conjunctival hæmorrhages ; swelling of lids ; symmetrical. Diagnosis : Koch-Week's conjunctivitis. Film and culture gave Koch-Week's bacillus.

In support of this it may be mentioned that towards the latter part of the series 35 of the cases presenting typical characteristics of Koch-Week's conjunctivitis were marked as "certain," and in every instance Koch-Week's bacillus was bacteriologically proved to be present. When all cases of Koch-Week's conjunctivitis are considered, there remain a large number in which the conditions are not perfectly

typical, but in which a correct diagnosis may usually be made by attention to the presence of several of the more important characteristics. (1) The age—the fact that so many of the cases occurred at the school period is important. (2) A short interval since onset of symptoms, such as from three or four to seven days. (3) A history of others being affected with similar symptoms. (4) The involvement of the ocular conjunctiva. (5) Muco-purulent discharge in fair amount. (6) The presence of conjunctival hæmorrhages. Conjunctival hæmorrhages occurred in 21·16 per cent. of the proved Koch-Week's cases; in 0·86 per cent. of the proved diplobacillary cases and in 8·8 per cent. of all other cases in which these organisms were not found. (7) Cases coming from rural districts are unlikely to be Koch-Week's cases, since in this series we have not met with one such case. It is mainly in the differential diagnosis between Koch-Week's conjunctivitis and the diplobacillary form that difficulties have arisen.

In the series of 820 cases of conjunctivitis a clinical diagnosis of the presence of Koch-Week's bacillus was made in 346 cases, and confirmed in 268 or 77·4 per cent. If the 32 cases which are still considered to have been due to this bacillus are included (*vide* p. 450), there are then 300 cases, *i.e.*, 87 per cent., in which we believe the clinical diagnosis was correct. Calculating from the number of times Koch-Week's bacillus was met with in the series, and the number of times a clinical diagnosis of this organism was made, we find that, out of 310 cases bacteriologically proved to contain Koch-Week's bacillus, a correct clinical diagnosis was made 268 times, *i.e.*, in 86·4 per cent. of cases.

Films.—These, made directly from the secretion of the conjunctival sac, were stained in a manner previously mentioned. Koch-Week's bacilli by this method are seen as fine rods about 0·5 μ to 1 μ in length, occasionally somewhat longer. At times two are joined end to end. Their ends appear somewhat rounded, frequently they are met with intracellularly. The cells of the secretion are some-

times seen to contain a number of these bacilli. There is nothing characteristic in this arrangement, for the bacilli are met with just as frequently extracellularly. In films where the bacilli are scanty a prolonged search may be necessary, and if bacillus xerosis is present, a doubt might arise whether the one or two slender rods met with are really Koch-Week's bacilli. It is here that the importance of staining the film by Gram's method becomes evident. It was our original intention to take two films from each case, one of which was to be treated by Gram's method with contrast staining by means of safranin. We found, however, that the amount of discharge in those cases in which a doubt was likely to arise was not sufficient to give two films as well as a culture.

Cultures.—The discharge for the culture was as far as possible taken from the conjunctival sac and not from that which had collected at the inner canthus. The former material was less likely to be contaminated with saprophytic organisms than the latter. The tubes, when inoculated, were transferred to the incubator with the least possible delay; at times, however, the interval elapsing before doing so has been an hour or two, and this we believe to be disadvantageous from the point of view of successful cultivation. These tubes were examined after at least 48 hours' incubation. Colonies of the Koch-Week's bacillus were visible, and presented an extremely minute dew-drop character, which was rendered more evident by examination with a low magnifiying power and resembled those described by Axenfeld.* When associated with the presence of one or two staphylococcus colonies these dew-drops were more conspicuous. With bacillus xerosis, whose colonies are much smaller than those of the staphylococcus, the prominence given to the Koch-Week's colonies was not so marked. In pure cultures, which have been obtained from time to time directly from the conjunctival discharge, Koch-Week's

* Handbuch der pathogenen Mikro-organismen, Kolle u. Wassermann, 1905.

colonies, although occasionally abundant, had to be carefully looked for. This prominence of Koch-Week's colonies in the neighbourhood of staphylococcus and xerosis colonies, so well marked in the case of the former, would lend support to the symbiotic view which has been put forward. In association with colonies of diplobacilli, colonies of Koch-Week's bacilli are not so conspicuous as when associated with either of the two former organisms, perhaps due to the greater contrast between the white and yellow colonies of the two former organisms as contrasted with the semi-transparent colonies of diplobacillus. Films were made from the cultures and stained by the Gram and safranine method already mentioned. Microscopically in such films the Koch-Week's bacilli were usually recognised without difficulty, the red stained slender rods contrasting with the larger red stained diplobacilli, the violet stained cocci or bacillus xerosis when present.

The *media* most suitable for the growth of this organism was ovarian agar. The ovarian fluid should be recently obtained. It was found that fluid containing from 5 to 7 per cent. of albumin, as tested by Esbach's albuminometer, also blood derivatives, the presence of which were proved by obtaining a spectrum of hæmochromogen, was most suitable for preparing the ovarian agar. After being kept for six months or thereby, ovarian fluid, although sterile, does not yield a satisfactory culture of Koch-Week's bacilli. When the series was begun, in 1905, the ovarian fluid employed was some six months old, and it was noted that the medium made was not furnishing satisfactory cultures of the bacilli. That the fluid was originally a good one cannot be doubted, for it was by the use of it in August and September of 1904 that Koch-Week's bacilli were isolated in pure culture and carried through 30 to 40 generations. It was suggested that light, since it exercises photo-chemical phenomena on certain fluids exposed to it, might have had a deteriorating influence on the fluid; it was therefore decided to keep the future fluids and prepared media in the dark. Fluid B (see

page 439), so stored, obtained on March 11, 1905, yielded successful cultures of Koch-Week's bacilli as late as October 11, that is seven months after it was obtained; it was then exhausted.

Other fluids which had been tried for the culture of Koch-Week's bacilli have in no instance been so successful as recently obtained brown viscid, ovarian fluid. Fluid E, a parovarian fluid, obtained on July 29, which contained no blood derivatives and only 0·15 per cent. of albumin, was quite unsatisfactory. Fluid D, an ascitic fluid from a case of tubercular ascitis, containing 4 per cent. of albumin and no blood derivatives, was so unreliable that its use had to be discontinued. Fluid J, a hydrocele fluid containing 5·5 per cent. of albumin and no blood derivatives, furnished fairly good cultures. Its use, however, was not continued, as for our requirements there was sufficient good ovarian fluid whose reliability could not be called in question. Blood-smeared agar was tried on several occasions. We have almost invariably failed to obtain cultures by this method, although the cases in which it was tried were those in which films of the discharge showed Koch-Week's bacilli. The agar was smeared with human blood taken from the finger, and also from the conjunctival vessels by the method suggested by Bishop Harman.* The latter procedure was, in our hands, unsatisfactory, inasmuch as it entailed needless discomfort to the patient and frightened children, in whom the majority of such cases occur.

Isolation of Koch-Week's Bacilli.—In September, 1904, during the epidemic of Koch-Week's conjunctivitis at the Industrial School before mentioned, cultures were taken from 12 cases. Eleven of the culture tubes showed colonies of the bacillus. Sub-cultures were made from each of these. Koch-Week's colonies were recognisable in most of the sub-cultures. In the remainder the saprophytic organisms had grown so profusely that isolation, by further sub-culture, would have been extremely difficult. It was

* The Conjunctiva in Health and Disease, p. 48.

decided to devote attention to those cultures in which Koch-Week's colonies were relatively numerous as compared with colonies of other organisms. Eventually, after a series of sub-cultures, this became narrowed down to dealing only with sub-cultures obtained from one of the cases. The organism was in this case growing along with the diplobacillus. Successive streaks were made on ovarian agar, and eventually Koch-Week's bacillus was obtained in pure culture. Mixing the impure culture with ovarian fluid, in Petri's dishes, thereafter adding liquified nutrient agar and incubating, failed as a means of isolation. The colonies of Koch-Week's were either so small and scattered, or so mixed up with the diplobacillus, that their isolation and recultivation was impossible. In the 24 hours' culture of the Koch-Week's bacillus and diplobacillus on ovarian agar, the diplobacillus colonies were evident by their round greyish semi-transparent appearance, whilst at intervals in the streaks were seen the minute, punctate, transparent, colonies of Koch-Week's bacilli. Similar cultures on ascitic agar presented no appreciable difference. Pure cultures of the Koch-Week's bacillus were made on ovarian agar and ascitic agar. They presented the same characters on both media; after 48 hours they were punctate, and even after nine days or longer in the incubator there was no appreciable increase in the size of the colonies. The colonies of Koch-Week's bacillus when grown alone were not appreciably different in size from those grown along with the diplobacillus, although the presence of the diplobacillus colonies served to draw attention to those of Koch-Week's. The Koch-Week's bacillus would not grow on agar medium. Petri's dishes with ovarian agar were streaked with, in one case, diplobacillus, in another case with bacillus xerosis, and in a third case with staphylococcus. These were then incubated for 24 hours. Successive streaks of Koch-Week's bacilli were then made on either side of the streaked cultures of the other organisms. Several streaks were in each instance made so as to vary in distance from

the staphylococcus and other colonies. These were thereafter incubated for 48 hours. On examination it was especially noticeable that the growth of Koch-Week's bacillus was in every instance most luxuriant in proximity to the streaks of the other organisms. It must, however, be stated that the streaks of Koch-Week's bacilli adjacent to the other organisms had in each instance been made before the more distant ones. The colonies adjacent to these streaks of other organisms were in no instance larger than those more distant. The pure culture of Koch-Week's bacillus was carried through nearly 40 generations. The later sub-cultures of Koch-Week's bacilli showed abundance of involution forms (photo 2), which were long and threadlike, and in other instances formed quite a tangled mass. In a 48 hours' culture, whilst these were abundant, in a 96 hours' culture they predominated still more, and after 10 days the thread forms were much broken up and there was an abundance of granular débris.

When a pure culture of Koch-Week's bacillus was obtained directly from the conjunctival discharge in cases occurring in the series taken in 1905, attempts were made from time to time to obtain sub-cultures. These were obtained, but they have shown a marked tendency to die out after the third or fourth generation. It is possible, then, that symbiosis may be of value in aiding the growth of the Koch-Week's bacillus. When repeated sub-cultures have been made of the bacillus in association with an organism such as the diplobacillus, it may have become so adapted to saprophytic conditions that when isolated therefrom, in a pure condition, it will then be capable of repeated sub-culture. Another medium employed for the growth of the Koch-Week's bacillus was citrated blood agar. This was prepared in the following manner. Into a litre flask, such as was before described, 2·5 grammes* of citrate of soda

* The amount was calculated from the proportion of lime and magnesium salts present as phosphates in blood; an excess of the citrate of soda was added.

dissolved in 20 c.c. of distilled water were placed. This was then sterilised, as also were a trochar and canula with long rubber tube attached to it. These were then taken to the slaughter-house; directly an ox was killed the skin and subjacent tissues were dissected up, the jugular vein exposed, and the canula inserted. The blood was then allowed to flow through the canula and tube. The first quantity being rejected, the flask was thereafter filled and replugged with the cotton wool. This citrated blood, which contained 0·25 per cent. of citrate of soda, was then mixed with nutrient agar in a manner similar to that already described for the preparation of ovarian agar. A rich red coloured medium was thus obtained. When Koch-Week's bacillus was streaked on such a medium the colonies were very readily visible to the naked eye, much more so than on any of the other media employed. As the ovarian agar, of which there was sufficient quantity, was quite satisfactory for the growth of Koch-Week's bacillus, and as it was thought that the citrated blood medium would be less reliable from the point of view of contamination, we did not continue to use it.

Out of 310 proved Koch-Week's cases a culture and a film were taken in 282. Both the culture and film showed the presence of the bacillus in 187 of them. In 82 of the 282 cases the film was positive and the culture negative. In 13 of the 282 cases the film was negative while the culture was positive. This gives a total of 200 cultures obtained. If the number of cultures in cases where no film was taken are included, we then find that the bacillus was obtained 232 times.

When the various media employed are compared and consideration given only to such cases as were proved by the film to contain Koch-Week's bacilli, it is found that of 39 inoculations of fluid A 16 were positive and 23 negative. The majority of the negative ones occurred when the fluid had been kept longer than six months. Of 55 inoculations on medium B 45 were positive and 10 were negative. This fluid was used only for a short time after it had been

obtained. On medium C of 58 inoculations 51 were positive, seven were negative. On medium D, of 14 inoculations five were positive and nine were negative; such a result led to the abandonment of this medium. On fluid E. of 17 inoculations six were positive and 11 were negative. This medium was then also abandoned. On medium F there were three inoculations, and all were negative. On medium G there were 44 inoculations with 33 positive and 11 negative. On medium H there were 35 inoculations with 28 positive and seven negative. On medium I, which was obtained towards the conclusion of the series, there were four inoculations, three positive and one negative.

Diplobacillary Conjunctivitis.

There were 274 bacteriologically proved cases of this form in the series of 820 cases of conjunctivitis.

Out of the 820 cases there were selected (1) all cases clinically diagnosed as due to the diplobacillus; (2) all bacteriologically proved cases of diplobacillary conjunctivitis. These were then grouped as follows:—

(1) Cases clinically diagnosed as due to the diplobacillus and bacteriologically confirmed; of such there were 176 cases. Of these, 171 diagnosed as due to the diplobacillus and confirmed bacteriologically are hereafter referred to as Group A. Five diagnosed as due to the diplobacillus in which both Koch-Week's bacillus and the diplobacillus were present are hereafter referred to as Group B.

(2) Cases clinically diagnosed as due to the diplobacillus in which bacteriologically that organism was not demonstrated. There were 78 cases, hereafter referred to as Group C.

(3) Cases wrongly diagnosed, in which the diplobacillus was shown bacteriologically to be present. There were 67 cases, hereafter referred to as Group D; 31 were diagnosed as Koch's-Week's conjunctivitis, 36 as "other forms."

In all, 321 cases were thus investigated. This does not include (1) the 26 cases diagnosed as due to Koch-Week's bacillus and bacteriologically shown to contain both Koch-Week's bacillus and the diplobacillus already dealt with under Group B of the Koch-Week's series and (2) five cases in Group D of the same series.

Subjective Symptoms.

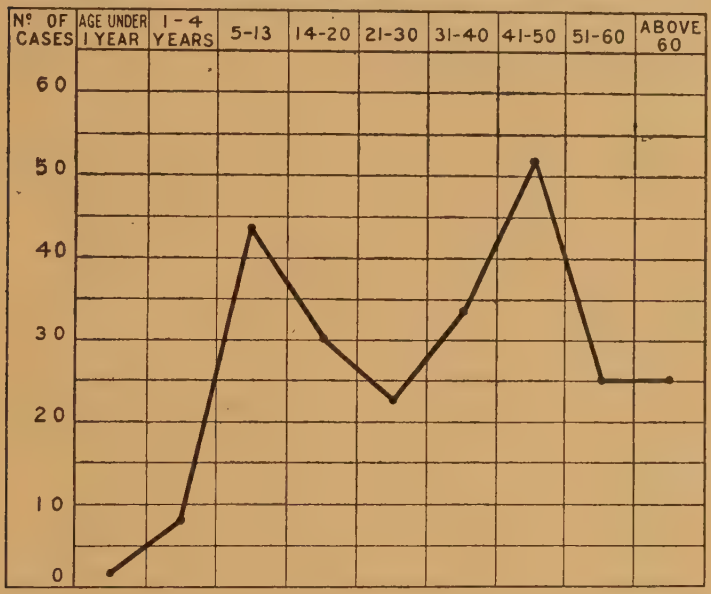
	Group.				
	A.	B.	C.	D.	A + D.
Grittiness, gumminess, or both ...	164	5	75	67	231
Difficulty in reading	15*	1	8†	1‡	16
Rainbows	1	1	1	0	1
Heavy lids	15	0	9	1	16
Other complaints	16	1	14	8	24

Age Incidence.

Age.	Group.				
	A.	B.	C.	D.	A + B + D.
Under 1 year	0	0	0	2	2
1—4 years	0	0	1	8	8
5—13 ,, ...	14	0	7	30	44
14—20 ,, ...	19	2	13	9	30
21—30 ,, ...	17	0	18	6	23
31—40 ,, ...	29	0	13	5	34
41—50 ,, ...	47	2	14	3	52
51—60 ,, ...	23	0	6	2	25
60 and upwards ...	22	1	6	2	25
Total cases ...	171	5	78	67	243

* Most of these were over 40 years of age.
† Six were under 40 years of age.
‡ Aged 12.

A table showing the number of proved diplobacillary cases at different age periods (it does not include 31 cases of diplobacillus, present with Koch-Week's bacillus, which were clinically diagnosed as Koch-Week's bacillus or "other forms") is shown graphically in the following chart:—



The number of cases under 14 years of age is 54. When those cases whose age was under 14 years are added from the 31 cases in which the Koch-Week's bacillus was associated with the diplobacillus (24), there are 78 cases in which the diplobacillus was found in children under 14 years of age.

Therefore children under 14 years of age were affected in 28·46 per cent. of the 274 cases in which the diplobacillus was demonstrated.

It is evident that the majority of cases of diplobacillary conjunctivitis occur in adults. There are, however, a considerable number to be met with in children, especially at the school period, and, in ignorance of this, a clinical diagnosis of this organism in children was seldom made,

especially during the first part of the inquiry. Of the 67 cases in Group D 40 occurred before the age of 14. Thus out of 54 cases of proved diplobacillary conjunctivitis in patients under 14 years of age only 14 were correctly diagnosed. Of the remaining 40, 31 were diagnosed as cases of Koch-Week's conjunctivitis. Out of 184 proved cases of diplobacillary conjunctivitis above the age of 13 years, 157 were correctly diagnosed.

Interval since Onset of Symptoms.

Interval.	Group.				
	A.	B.	C.	D.	A + D.
Under a week	30	1	18	40	70
14—21 days	51	1	23	13	64
28 days to 3 months ...	63	2	23	12	75
Longer	24	1	14	1	25

(Cases occurring between one week and 14 days, also between 21 and 28 days, are intentionally omitted.)

On comparing Groups A and D it will be seen that whereas in Group A with 171 cases 30 came within a week of the onset of symptoms, in Group D with only 67 cases there were 40 which came at a corresponding period. It should be noted in Group A that of the 30 cases which came not later that one week after onset of symptoms, 27 were adults, and three children. On the other hand, in Group D, of the 40 cases which came not later than one week after onset of symptoms, 30 were children and 10 adults.

When Groups A and D are combined it will be seen that of 238 cases of diplobacillary conjunctivitis 70 came within a week of onset of symptoms, 37 adults, 33 children. Of the 238 cases, without reference to onset of attack, 54 occurred in children, 184 in adults. It is, then, apparent that the interval between commencement of symptoms and the time when advice is sought is shorter in the case of children than it is in adults.

Previous Attacks.

A—48, B—0, C—30, D—21.

In Groups A and D, which together amount to 248 cases of proved diplobacillary conjunctivitis, 69 had previous attacks. (In Koch-Week's cases this was true of 33 in 284 cases.) On February 28, 1906, diplobacilli were present in a film taken from the discharge of an individual in whom this organism had been found on July 21, 1905.

Others Affected with the same Symptoms.

	Group.				
	A.	B.	C.	D.	A + D.
In same house	35	4	11	21	56
Elsewhere	5	0	4	8	13

Increased Redness of Conjunctiva.

	Group.				
	A.	B.	C.	D.	A + D.
Ocular and palpebral ...	72	2	37	51	123
Palpebral alone	99	3	41	16	15

Amount of Conjunctival Discharge.

	Group.				
	A.	B.	C.	D.	A + D.
Scanty	139	1	66	50	189
Moderate	32	4	12	16	48
Profuse	0	0	0	1	1

Character of Discharge.—The discharge, as in cases of Koch-Week's conjunctivitis, was of the usual muco-purulent character.

Presence of Enlarged Conjunctival Follicles.

Group A—16, B—0, C—5, D—12.

Presence of Conjunctival Hæmorrhage.

Group A—1, B—0, C—2, D—1.

The ages of these cases were respectively 41, 34 and 51, 41.

Presence of Swelling of Lids.

Group A—97, B—3, C—37, D—52.

Neither *Chemosis* nor *membrane* was present in a single case of any of the groups.

Presence of Enlarged Preauricular Gland.

Group A—22, B—1, C—3, D—20.

Angular Conjunctivitis was considered to be present when in association with a conjunctivitis there occurred increased redness of the edge of the lid, limited to its outer or inner end, or when in addition there was increased redness of the skin at either the outer or inner canthus. This condition was noted, when present, in every case from July 1 to December 31, 1905. Four hundred and forty-two cases of conjunctivitis were examined during that period, 121 of these were diplobacillary cases. In 42 of the 442 cases of conjunctivitis angular conjunctivitis was noted; in 37 of these the diplobacillus was found, *i.e.*, in 34·7 per cent. of the diplobacillary cases.

The remaining five cases are:—

Case 339 (exophthalmic goitre), with signs present at the inner canthus, a film and culture yielded only xerosis bacillus and staphylococcus pyogenes aureus and albus; the medium was satisfactory.

Case 455 had this symptom present at both inner and outer canthi, and in a film xerosis bacillus was found, and in culture staphylococcus pyogenes aureus and albus, the medium was unsatisfactory.

Case 652 had the outer canthus affected, no film was taken, culture yielded staphylococcus pyogenes aureus and albus; the medium was good.

Case 740 had the inner canthus affected, no culture. Two films were taken, but no organism was found in them.

Case 794 had signs at the inner canthus; Koch-Week's bacillus was found in the film along with staphylococcus pyogenes aureus and albus in the culture; medium good. It may be noted that in cases 740 and 455 there is a possibility of the diplobacillus having been missed, but as regards the other three cases this is not likely.

In 16 of the 37 cases with angular conjunctivitis occurring in diplobacillary cases the characteristic appearance was present both at the inner and outer canthus. In 18 cases it occurred at the inner canthus, the outer being unaffected. In three cases it occurred at the outer canthus, the inner being unaffected.

Though not systematically noted, it was remarked that several of these cases complained of itching at the outer and inner canthus, causing them to rub these situations.

Conclusions.

(1) Angular conjunctivitis occurs in about one-third of all conjunctivitis cases due to the diplobacillus.

(2) When angular conjunctivitis is present it is almost pathognomonic of the presence of the diplobacillus. In 88 per cent. of our cases of angular conjunctivitis this micro-organism was found.

Proportion of Uniocular to Symmetrical Cases.

	Group.				
	A.	B.	C.	D.	A + D.
Uniocular	8	0	4	17	25
Symmetrical	163	5	74	50	213

Presence of Corneal Ulcers, etc.

	Group.			
	A.	B.	C.	D.
Corneal ulcers	3	0	3	3
Impetigo	0	0	0	2
Phlyctenules	0	0	0	4
Nasal and aural discharge ...	0	0	0	0

Clinical Diagnosis.—In the clinical diagnosis of diplobacillary conjunctivitis, as in the case of Koch-Week's conjunctivitis, subjective symptoms are of but little value as a means of distinguishing the micro-organism. Either grittiness or gumminess of the lids or both are complained of in nearly every case. It may be mentioned, however, that of 238 proved cases of diplobacillary conjunctivitis, 16 complained of heaviness of the lids, and of the cases which were clinically diagnosed as due to the diplobacillus, though not bacteriologically confirmed, nine made the same complaint. In seven of these we should yet make a similar clinical diagnosis. There are possibilities of the micro-organisms having been overlooked for various reasons previously given under Koch-Week's conjunctivitis. As illustrating the slightness of the subjective symptoms, cases have been met with in which the patient came on account

of some condition other than conjunctivitis, *e.g.*, Case 544, which came on account of corneal injury, and Case 357, which came on account of advanced cataract. Again, in one member of a family who had had no subjective symptoms for some time, and in whom there were no objective signs of conjunctivitis, diplobacilli were obtained from the conjunctival sac. She was examined because her three sisters and mother, living in the same house, had unmistakable signs of conjunctivitis, and in each of them the diplobacillus was found. This case is not one of the series. Diagnosis must therefore rest mainly upon a grouping of age, history—previous attacks, interval since onset of attack, etc.—and objective symptoms.

Age.—Too much stress must not be laid on the age. In 171 cases clinically diagnosed and bacteriologically proved to be due to the diplobacillus, 99 occurred between the ages of 31 and 60. If we add those over 60 years of age, there is a total of 121. On the other hand, in those cases (67) wrongly diagnosed but bacteriologically proved to be due to the diplobacillus, 40 were under the age of 14. If these two groups be combined it is found that of 238 cases of diplobacillary conjunctivitis, 54 were under 14 years of age and 133 over 30; this indicates how important it is to recognise that diplobacillary conjunctivitis is by no means infrequent in children. When all the cases in which the diplobacillus was present with the Koch-Weck's bacillus are included, the figures show that 78 children out of 274 diplobacillary cases were affected, 28·46 per cent.

Gonin* found in Lausanne that diplobacillary conjunctivitis was rare in children. Axenfeld† states that the age varies between 10 and 57. Stephenson‡ states that it may occur at any age, even in newly born babies.

* Revue de la medicale de la Suisse-Romande (Fevrier et Mars, 1899). Reviewed in the Annales d'Oculistique, 1899, p. 78.

† Centralblatt für Bacteriologie Parasitekunde u. Infectionskrankheiten, vol. xxi, No. 1, January, 1897.

‡ Contagious Ophthalmia, p. 27.

Whilst a difficulty may arise in the differential diagnosis of Koch-Week's from diplobacillary conjunctivitis at the school period, such a difficulty can seldom occur in patients over 40 years of age, since in our series there are only two cases of Koch-Week's conjunctivitis—one of these had the diplobacillus associated—above that age, whilst diplobacillary conjunctivitis predominates at or beyond this age over every other form of conjunctivitis.

Interval Since Onset of Symptoms. — As regards the duration of the interval between the onset of symptoms and the patient's first visit, this to a certain extent varies with the age of the patient, for whilst in the majority of adults an interval ranging from 14 days to three months elapsed, in most of those at the school period the interval was shorter, generally about one week or thereby.

Previous Attacks, though not recorded in a large number of cases, are of sufficient frequency to be of diagnostic importance. They were noted in 61 of the 238 proved cases of diplobacillary conjunctivitis, and 30 times in the 78 unconfirmed cases. Of these latter, 13 from their clinical features would still be diagnosed as due to the diplobacillus. In two the diagnosis is almost certainly wrong. In 15 a diagnosis could only be made at random.

Others Affected.—The statement that others are affected is of little importance, from the fact that a large proportion of Koch-Week's cases give this history. In a case where there is doubt as to the differential diagnosis between Koch-Week's and diplobacillary conjunctivitis, the balance would be turned in favour of the conjunctivitis being due to the Koch-Week's bacillus by the fact that others were affected.

An example of the infectious nature of diplobacillary conjunctivitis is case 804, one of diplobacillary conjunctivitis, which attended on December 20, 1905. On the 27th of the following January her sister, aged 12, came, presenting symptoms which were characteristic of conjunctivitis caused by the diplobacillus. This micro-organism was found. This

is still better seen in the instance already mentioned in which five members of a family in the same house were affected with diplobacillary conjunctivitis; also in a family examined in March, 1906, in which the mother, a son and a daughter were bacteriologically proved to have diplobacillary conjunctivitis. Stephenson* mentions an outbreak of this form of conjunctivitis which affected about a dozen children.

Congestion of the Conjunctiva.—In about half of the proved cases of diplobacillary conjunctivitis (115 out of 238 cases) the palpebral conjunctiva alone was congested; this contrasts remarkably with Koch-Week's conjunctivitis, in which 33 out of 310 cases had the congestion limited to the palpebral conjunctiva. In children, however, according to our figures when only the palpebral conjunctiva is congested, the case, viewed from this symptom alone, is more likely to be one of Koch-Week's conjunctivitis than of diplobacillary, for of the 33 cases (palpebral conjunctiva alone affected) which occured in the Koch-Week's series, 23 occurred in children, whilst of the 115 cases which occurred in the diplobacillary series only 16 were in children. If infants are excluded the result is reversed—14 cases are due to the diplobacillus and 12 to Koch-Week's bacillus. It must, however, be borne in mind that there were 257 children with Koch-Week's conjunctivitis as against 54 with diplobacillary. While therefore the chances of a case of conjunctivitis in a child are very strongly in favour of its being due to Koch-Week's bacillus, these chances are greatly diminished when the palpebral conjunctiva alone is congested.

Amount of Discharge.—In the majority of proved diplobacillary cases the quantity of conjunctival discharge is small, 189 of the 238 cases. Of the 48 cases with a moderate quantity of discharge (Groups A and D) 14 occurred in children.

* *Loc. cit.*

Enlarged Follicles.—Enlarged follicles occurred in 20 of the 238 proved cases. Nine were in children and three in adolescents. In the cases of Koch-Week's conjunctivitis (310) there were 43 with enlarged follicles, of whom 38 were in children.

Conjunctival hæmorrhages, though rarely met with, do not exclude the possibility of a conjunctivitis being due to the diplobacillus; for in Case 469, an adult, aged 41, with symptoms present for two months prior to his seeking advice, the presence of the diplobacillus, which had been diagnosed, was confirmed by a film and culture. Conjunctival hæmorrhages were present. Also case 708, a patient aged 41, with symptoms for eight days, and with conjunctival hæmorrhages present. The conjunctivitis was not diagnosed as due to the diplobacillus, but this micro-organism was demonstrated in the culture. No film taken.

The presence of *chemosis or of membrane* on the conjunctiva would almost certainly exclude a diplobacillary conjunctivitis, for in none of the cases in the four groups A, B, C, D has either of these conditions been met with.

Swelling of the lids is noted in the majority of cases. In most instances it is much less marked than in the Koch-Week's cases.

Enlargement of the preauricular gland is less frequent in diplobacillary than in Koch-Week's conjunctivitis.

A *uniocular* diplobacillary conjunctivitis is uncommon (25 in 238). The interval since onset of the symptoms in the majority of these cases was short, in 15 of the 25 cases not longer than seven days; 12 of the 17 uniocular cases which were not diagnosed as diplobacillary conjunctivitis, but which proved to be so, occurred in children. In nine of these, symptoms had lasted not longer than seven days. We failed to diagnose a single case of uniocular diplobacillary conjunctivitis in children. A uniocular diplobacillary case which presented difficulty in deciding whether to include it in the series was—

Case 466, a male, aged 62, with a conjunctivitis of his left eye resembling that due to the diplobacillus, which micro-organism was proved to be present. The right eye showed no evidence of conjunctivitis, but the lower canaliculus was found to have been opened, and there was regurgitation of muco-pus from the sac when pressure was made on it. Pneumococci were proved by culture and animal inoculation to be present in the discharge from this lachrymal sac.

Corneal ulcers are met with in typical as well as atypical cases. They are noted six times in 238 cases which were bacteriologically proved to contain diplobacillus in the conjunctival discharge.

Character of the ulcers. In case 305 there were two small grey circular superficial ulcers near the outer margin of the right cornea. In case 281 there was a circular grey ulcer near the inner lower corneal margin. In case 544 the ulcer resulted from injury. In the remaining three cases (174, 102, 517) no details were given.

Of the four cases in which *phlyctenules* are noted, three occurred in children. In no single instance was a correct diagnosis of the diplobacillus made.

Angular conjunctivitis when present is almost pathognomonic, *vide* p. 469.

Based on a combination of these clinical features, it is possible to make a diagnosis with considerable exactness in the majority of cases of diplobacillary conjunctivitis especially when affecting adults. Thus of the 171 cases diagnosed correctly, 158 were in adults, whilst of the 67 wrongly diagnosed only 27 were in adults. A correct diagnosis is not so easily made in children, but our figures no doubt show a much higher percentage of failures in diagnosis than will result when it is appreciated with what frequency the diplobacillus occurs at this period of life. Of 54 cases of diplobacillary conjunctivitis in children a correct diagnosis was made only 14 times. A clinical diagnosis of Koch-Week's conjunctivitis was made in 19 of

the 54 cases, showing how the two varieties may resemble each other at this age.

Typical cases present little or no difficulty in diagnosis. In support of this, during the latter part of our inquiry, 18 cases presenting features supposed to be unequivocal were diagnosed clinically as diplobacillary conjunctivitis and marked "certain." In every instance the diagnosis was bacteriologically confirmed.

As typical cases of diplobacillary conjunctivitis we may cite—

Case 696, a female, aged 46, living in town, complaining of a gritty feeling in her eyes and gumminess of lids for 14 days; previous attacks; no others affected; only palpebral conjunctiva congested; discharge scanty; swelling of lids; symmetrical; angular conjunctivitis. Diagnosis: diplobacillus; film and culture gave diplobacillus.

Case 758, a female, aged 65, resident in town, difficulty in reading, gritty feeling in eyes and gumminess of lids for three months; no previous attacks; no others affected; only palpebral conjunctiva congested; discharge scanty; swelling of lids; symmetrical. Diagnosis: diplobacillus; culture and film gave diplobacillus.

Case 820, male, aged 41, resident in country, difficulty in reading, gritty feeling in eyes and gumminess of lids for three months. Previous attacks; no others affected; palpebral and ocular conjunctiva congested; discharge scanty; symmetrical; angular conjunctivitis. Diagnosis: diplobacillus; film and culture gave diplobacillus.

When all cases of conjunctivitis due to the diplobacillus are considered, there is a large group in which a diagnosis should be made with considerable certainty when based on a consideration of the various clinical characters, viz.:—

(1) Angular conjunctivitis, which occurs in about one-third of the cases and is almost pathognomonic.
(2) Age.
(3) Interval since onset of symptoms, which is of long duration in adults.

(4) Congestion frequently limited to the palpebral conjunctiva.
(5) Scanty discharge.
(6) Absence of conjunctival hæmorrhages.
(7) A history of previous attacks.
(8) Cases coming from rural districts.
(9) Complaint of heavy lids.

In our series a diagnosis of diplobacillary conjunctivitis was made in 254 cases. In 176 of these, bacteriological confirmation was obtained—69·3 per cent. Viewed on the other hand from the bacteriological standpoint, of 243 proved diplobacillary cases 176 were correctly diagnosed, *i.e.*, 72·4 per cent.

Of the 78 cases wrongly diagnosed as due to the diplobacillus, seven proved to be due to Koch-Week's bacillus; six of these, the youngest of which was eight and the oldest 40 years of age, on reconsideration of their schedules, would still be diagnosed in a similar manner; this illustrates the impossibility in certain cases of differentiating clinically a Koch-Week's from a diplobacillary conjunctivitis. In the 7th case it would be difficult to form a diagnosis. A patient, aged 29, with symptoms present for four days; no previous attacks; no others affected; palpebral and ocular conjunctiva congested, a moderate quantity of discharge, lids swollen, and the condition uniocular. Diagnosis: diplobacillus. Film: Koch-Week's bacillus. Culture: Koch-Week's bacillus, staph. alb. and xerosis bacillus. The age is against the probability of its being Koch-Week's conjunctivitis, whilst the other conditions are compatible with a conjunctivitis due to either organism.

Nine of the 78 wrongly diagnosed cases were bacteriologically shown to contain *pneumococcus*; eight of these we should still diagnose as diplobacillary cases, as the clinical features are identical. The remaining one, Case 416, may have been a lachrymal one, in which case it should have been omitted. A female, aged 77, with symptoms present for

12 months, a history of others affected, congestion limited to the palpebral conjunctiva, scanty muco-purulent discharge, both eyes affected, with the right lower canaliculus slit.

Organisms were not demonstrated in six cases; in four of these no film was taken, and in another no culture was taken. In the six cases there is reason to believe that the diplobacillus was present, though the organism was not found. In support of this view, it may be noted that in five of the six cases only a film or a culture was taken, and that in all of these the quantity of discharge was small.

"*Other forms*" were found in 56 cases.

The difficulties of diagnosis, owing to treatment having been employed, is exemplified by the following:—

Case 814, a male, aged 25, with subjective symptoms of conjunctivitis present for 28 days, previous attacks, palpebral conjunctiva alone affected, discharge scanty; symmetrical, using "golden ointment." Diagnosis: diplobacillus. Film: cocci. Culture, nil.

Although there was no conjunctival discharge when seen by us, the next case was considered to be one of conjunctivitis due to the diplobacillus, but it was recognised that it might be impossible to obtain the specific organisms.

Case 779, a female, aged 63, complaining that the lids felt heavy, that they were gummed together in the morning, and that she had a feeling of sand in her eyes; symptoms had been present for two months, previous attacks, only palpebral conjunctiva congested, no discharge, symmetrical. Diagnosis: diplobacillus. Film: cocci. Culture: staphylococcus pyogenes aureus. For a similar reason, Case 776 was regarded in the same light.

During the latter part of our inquiry the rather frequent occurrence of diplobacillary conjunctivitis in children was recognised, and it was supposed that the following case belonged to this category. The diagnosis, however, of that organism was not confirmed; this shows the difficulty to be met with in arriving at a diagnosis in children.

Case 688, a female, aged 13, with the usual subjective symptoms of conjunctivitis for 14 days, previous attacks, only palpebral conjunctiva congested; discharge scanty, no others affected; symmetrical. Diagnosis: diplobacillus. Film: cocci. Culture, streptococcus pyogenes, staphylococcus pyogenes albus and aureus.

A somewhat puzzling combination of clinical characters was presented by Case 401, in which a diagnosis of the diplobacillus was made. In this case, in favour of the diagnosis of diplobacillus were the age, 34, residence in the country, previous attacks, and angular conjunctivitis. Against the diagnosis were the presence of conjunctival hæmorrhages, a moderate quantity of discharge and the short duration of symptoms—three days; it was symmetrical. Nothing but cocci was found. There was no culture.

In three of the 56 cases a diagnosis would be impossible. In four a diagnosis other than diplobacillus would be made, and in 49 the diagnosis would remain unchanged. Frequently cases are met with which are almost certainly due to the diplobacillus, but in which the discharge is either absent or so scanty at the time of examination that a sufficient supply of material for a satisfactory film or culture is not obtainable. The majority of these 49 cases belong to such a group.

Of the 67 cases wrongly diagnosed, which proved to be due to the diplobacillus, 31 were diagnosed as Koch-Week's conjunctivitis, and 19 of these were in children. Fourteen occurred in the early part of the series. On a reconsideration of the notes of these cases, it was found that the following case had points in favour of both Koch-Week's and diplobacillary conjunctivitis:—

Case 708, a female, aged 41, with symptoms of conjunctivitis for eight days, no previous attacks, others affected in the same house, both palpebral and ocular conjunctiva congested, scanty discharge, conjunctival hæmorrhages, swelling of lids, symmetrical. Diagnosis: Koch-Week's bacillus. The age and scanty discharge were the two conditions in favour of diplobacillary conjunctivitis, all the other conditions pointed to a Koch-Week's

conjunctivitis; no film was taken; in culture, diplobacillus and staphylococcus pyogenes albus.

That the clinical characters of diplobacillary conjunctivitis in a child may resemble those of Koch-Week's conjunctivitis is evident from this case—

Case 580, a child, aged 9, symptoms of conjunctivitis for 14 days, no previous attacks, palpebral and ocular conjunctiva congested, moderate quantity of discharge, lids swollen, preauricular gland enlarged, symmetrical. No film taken; in culture diplobacillus and staphylococcus pyogenes albus; also

Case 201, a child, aged 9, symptoms for two days, others affected in the same house, palpebral and ocular conjunctiva congested, scanty discharge, swelling of lids, preauricular gland enlarged, symmetrical, no film taken. In culture, diplobacillus and staphylococcus pyogenes albus; and

Case 431, a child, aged 12, with symptoms for four days, palpebral and ocular conjunctiva congested, a moderate quantity of discharge, swelling of lids, symmetrical, film and culture showed diplobacillus.

In eight of the 31 cases diagnosed as Koch-Week's conjunctivitis a different diagnosis would now be made. In three a diagnosis would be quite uncertain. In the remainder (20) the diagnosis would be unchanged. These, except two, were in children, which accentuates the difficulties of differentiating the two affections at this period.

Thirty-six cases diagnosed as "other forms" proved to be due to the diplobacillus. A few of these are as follows:—

Case 600, an infant of 3 weeks, with a history of discharge from both eyes since birth, palpebral and ocular conjunctiva congested, lids swollen, scanty discharge, symmetrical. Diplobacillus present in film and culture. Of four non-gonorrhœal cases occurring within the first few weeks of life, three were due to Koch-Week's bacillus and one to the diplobacillus.

Case 661, a syphilitic child in a much neglected condition, would give rise to insuperable difficulties in the clinical diagnosis

of the micro-organism which caused the conjunctivitis. A female, aged 4 months, with a history that the eyelids had been gummed together in the morning for the last two and a-half months, profuse conjunctival discharge, palpebral and ocular conjunctiva congested, lids swollen, symmetrical. The diagnosis of the micro-organism present was "other forms." In film, diplobacillus cocci and xerosis bacillus were present. In culture, staphylococcus pyogenes albus, aureus and xerosis bacillus.

It is believed that 21 of the 36 cases would now be diagnosed as diplobacillary. Of these 21 cases seven were in children, who had had previous attacks; 20 of them had scanty discharge; eight had symptoms present for a week or less. Five of the 36 cases would now be diagnosed as Koch-Week's conjunctivitis. In the remainder the evidence is so conflicting that a right diagnosis would be impossible, except by chance.

Bacteriology.—The discharge from cases in this group is frequently very scanty and is almost invariably poorer in cells than is the discharge from cases of Koch-Week's conjunctivitis. It is surprising how frequently the bacilli are found in relatively enormous numbers as compared with the number of cells. The material for a film may quite suitably be taken from the discharge collected at the caruncle. Good films can often be obtained in cases with no apparent discharge, by merely running the platinum loop over the caruncle and its neighbourhood. Bacilli when present in moderate numbers give rise to no difficulty in identification, but when few in number and when the bacillus xerosis is also present, one may at times have doubt. The bacillus xerosis, whilst smaller, sometimes resembles a diplobacillus. It is in such circumstances that the value of staining a film by Gram's method becomes apparent; still the recognition of one or two diplobacilli in a film would suffice for the diagnosis. The number of micro-organisms stands in no relation to the amount of discharge. Thus a scanty discharge may be teeming with micro-

organisms, whilst a moderate discharge may require careful searching of the film before the discovery of isolated diplobacilli. The bacilli are generally situated extra-cellularly, less frequently they occur intra-cellularly. They are from 2 to 4 μ in length and 1 μ in breadth. There may be two together joined end to end. We have never seen them arranged in chains. Their ends are rounded. Polar staining has not been noticed. They are not stained by Gram's method.

Cultures.—On ovarian agar after 24 hours at 37° C. round, elevated, semi-transparent, greyish colonies are readily visible. After 48 hours the increase in size is considerable, and frequently large colonies are met with displaying a pronounced central mammilla, with a greyish semi-transparent area around it. Such colonies are diagnostic. They are by no means constant. This cannot be due to defects in the media, for they have appeared on ovarian agar which was not giving satisfactory results with Koch-Week's bacilli, nor do the bacilli differ in mammillated from those in the other colonies. The mammillated colonies are almost invariably larger than the non-mammillated ones. Cultures after 48 hours may show abundance of involution forms (Photos. 4, 5, 6, 7, and 8). In older cultures their presence is constant. Sub-cultures from mammillated colonies do not reproduce this condition, which, in our experience, is limited to cultures made directly from conjunctival discharge. That the diplobacillus produces liquefaction of inspissated serum was shown repeatedly.

Of 238 bacteriologically proved cases of diplobacillary conjunctivitis, both a film and a culture were taken in 175; in these, 15 times the film and 12 times the culture gave a negative result. In cases with scanty or no discharge there is no evidence to show that a preference is to be given for a film rather than a culture, or *vice versâ*. In 19 of the 238 cases only films were taken, in 44 only cultures.

In the 78 cases diagnosed as due to the diplobacillus but not confirmed, 7 were shown to be due to Koch-Week's

bacillus and 9 to the pneumococcus. Of the remaining 62, in 38 both a film and a culture were taken, and in 32 of these discharge was scanty or absent. In 5 only a film was taken. In 19 only a culture. In all the discharge was either scanty or absent. In the 6 cases where no organism was found the discharge was scanty or absent. In only one of them was both a film and a culture taken. In Case 740, with angular conjunctivis, a film only was taken. As previously stated (*vide* pp. 478, 479), we now believe that 55 of the 62 cases were, in all probability, diplobacillary cases.

Gonorrhœal Conjunctivitis.—Of the 820 cases in the series, 21 were diagnosed clinically as due to the gonococcus; 18 of these were bacteriologically confirmed. Of the other 3, 1 was due to the diplobacillus and 2 to "other forms." In every case in which gonococci were found, a correct clinical diagnosis had been made. All the cases were in infants. Their ages ranged from 3 days to 2 months. Groenouw* investigated 100 cases of ophthalmia neonatorum and never once met with the diplobacillus.

In each of the 18 proved gonococcus cases the specific micro-organism was present in the film.

In 14 of the 18 cases a culture was taken, and in every instance a growth of the gonococcus was obtained.

As indicative of the facility with which growths of the gonococcus can be obtained on ovarian agar, in 24 cases (including the 14 already mentioned) in which a film showed the presence of the gonococcus, a culture was invariably obtained. The cultures maintained their vitality well, so that an indefinite number of sub-cultures could be obtained with ease.

The media for the growth of the gonococcus should be ovarian agar, hydrocele, or ascitic agar. The presence of blood derivatives is not essential.

Appearance of the culture:—After 24 hours' incubation at a temperature of 37° C., the gonococcus colonies are quite

* Die Augenentzündung der Neugebornen in klinischer u. bacteriologischer Hinsicht. Archiv f. Ophthalmologie, vol. lii, S. 1, 1901.

evident. After 48 hours, a luxuriant growth is present. The colonies are rounded, elevated, and semi-transparent, and have a grey appearance.

Tubercular Conjunctivitis.—The only case which occurred in the series, Case 419, was a female, aged 17, a farm worker, occupied chiefly in tending cows, with a history of redness and swelling of the right eyelids for three months, also gumming of the lids in the morning. There had been no pain. There was no difficulty, from the aspect of the conjunctiva, in making a diagnosis of tubercular conjunctivitis. There was also a depressed, bluish scar over the right preauricular gland. A swelling in this region had been previously lanced. Scrapings were taken and films made from the diseased conjunctiva. They were stained in the usual manner for tubercle bacilli, and after a prolonged search a single tubercle bacillus was found. The diseased conjunctiva was scraped and cauterised.

To clinch the diagnosis, a small piece of the affected tissue was inoculated in the groin of a guinea-pig. About five weeks later the groin glands were much enlarged, and there was an ulcer at the site of inoculation. After living for two weeks longer the animal was killed. The *post-mortem* examination showed several large superficial inguinal glands. The deep inguinal glands were also enlarged. The spleen was studded with tubercular nodules. The liver showed one or two nodules. In the lungs, especially the right one, were a number of tubercular deposits. Microscopically the affected tissues were found to contain numerous tubercle bacilli. A rabbit was also inoculated with a piece of the patient's affected conjunctival tissue. Generalised tuberculosis resulted.

On December 30, five months later, the patient reported herself, stating that she had no trouble with the eye. There was extensive scar tissue in the upper palpebral conjunctiva, but apparently no active disease.

Diphtheritic Conjunctivitis was met with once. Case 502, a male child, aged 2, was brought on account of "sore eyes."

The patient looked ill. Palpebral and ocular conjunctiva of both eyes were congested, and there was a moderate amount of muco-purulent discharge. A membrane extended over the whole of the left lower palpebral conjunctiva. Most of it was separated off by a platinum loop, with only a slight amount of bleeding. The conjunctiva thus exposed had a greyish appearance. A film was made; bacilli were present which resembled diphtheria bacilli. A culture gave colonies of diphtheria bacilli. A guinea-pig was inoculated with the culture material. Death resulted after 48 hours. The tissues were thickened at the site of inoculation, and, on removal of the skin in this region, numerous hæmorrhages were seen. The adjacent glands were not markedly enlarged. The suprarenal glands were congested.

Subsequent course of the case: two days after the first visit the lids of the patient were somewhat swollen and the membrane extended over the conjunctiva of the upper and lower lids. He was removed to the fever hospital. Antitoxin was administered and an uninterrupted recovery ensued.

Conjunctivitis not Proved to be Due to a Specific Organism.—After considering these various groups, there remain 114 cases in which a correct clinical diagnosis of "other forms" was made. The ground for making such a diagnosis was that, for various reasons, the conditions present made the isolation of a specific organism unlikely. The cases in this group are all of an atypical variety. A number had been rendered so by treatment with drugs, others by the eyes having been tied up. There was often an unreliable history, and random statements were made as to previous attacks and others affected. A number of the cases were young children sent by themselves. It is also to be remembered that a second bacteriological examination was not made in our cases. In 72 of the cases the affection was limited to one eye. In such cases symptoms had often been present for a long time. In nine of them the eye had been tied up, and, but for this circumstance, a diagnosis of Koch-Week's conjunctivitis would have been made. Example,

Case 729, a female, aged 9, with symptoms of conjunctivitis for 11 days; palpebral and ocular conjunctiva congested; moderate discharge; swelling of lids; uniocular. The affected eye had been tied up. Diagnosis: "other forms." Film: cocci; culture: streptococcus pyogenes and xerosis bacillus. Similarly,

Case 595, female, aged 9, with symptoms of conjunctivitis for a month, no previous attacks, palpebral and ocular conjunctiva congested, scanty discharge, lids swollen, uniocular, eye tied up. Diagnosis: "other forms"; no film taken; culture: staphylococcus pyogenes albus and aureus. It might be suggested that the tying up of the eye acted as a shield which prevented the affection spreading to the other eye; further, that the retention of the discharge under such suitable conditions as warmth and moisture, which favour the growth of organisms, caused so great proliferation of saprophytes that the relative proportion of the specific organism is diminished to such an extent that, on culture media, the luxurious growth of the non-specific organism chokes out the specific germ. As regards the value of films in such cases, it is suggested that the diminution of specific organisms, coupled with the marked increase in cellular elements, makes the number of such micro-organisms so small that their recognition is impossible. In none of the proved Koch-Week's cases is there an uniocular conjunctivitis in which the eye has been tied up.

After discounting as far as possible the elements of error, and reconsidering the cases, it seems reasonable to suppose that of the 114 :—

(1) Forty-seven were cases of Koch-Week's conjunctivitis, *e.g.*, Case 8, a female, aged 12, with sore eyes for a week, previous attacks, others affected in the same house and elsewhere, only palpebral conjunctiva congested, scanty discharge, symmetrical. Diagnosis: "other forms;" no film taken; culture: staphylococcus pyogenes albus and streptococcus.

(2) Thirty-five were cases of diplobacillary conjunctivitis, *e.g.*, Case 92, a male, aged 33, complaining that his lids felt heavy and that he had difficulty in reading for three months; previous attacks, palpebral conjunctiva congested, scanty muco-purulent

discharge, enlarged follicles, symmetrical. Diagnosis: "other forms;" no film taken; culture: staphylococcus pyogenes albus.

(3) Two might be due to either of these organisms, and

(4) the remaining 30 are impossible of diagnosis. Some of these possibly should not have been included in our series. Some were in-patients who were engaged in dusty occupations.

Cases in which no Micro-organisms were Found.—Some of these had marked objective signs of conjunctivitis. On the other hand, in certain of the cases these signs were doubtful, as at most there was only very slight discharge and increased redness of conjunctiva. In such cases the diagnosis of conjunctivitis was confirmed by the history. As showing the importance of the history in making a diagnosis of conjunctivitis, we may note the case of a female child, aged 11 months, with a history of gumminess of lids for two days, others affected in the same house. Objectively there was only increased redness of the palpebral conjunctiva and hardly any discharge. Koch-Week's bacillus and the diplobacillus were found in both the film and culture. In another case, a child, aged one, there was scanty or no discharge, and the palpebral conjunctiva was reddened. These were the only objective signs. There was a history of the lids being gummed for one day, and of others in the house and elsewhere being affected. Koch-Week's bacillus and the diplobacillus were found.

Pneumococcus.—In 24 cases of the series diplococci were found unassociated with either Koch-Week's bacillus or the diplobacillus. Eight were diagnosed clinically as Koch-Week's cases, 9 were diagnosed as being due to the diplobacillus and 7 as "other forms"; on reconsideration of the latter, 6 we believe may have been Koch-Week's cases, and 1 a case due to the diplobacillus. Grouped in this manner, 14 presented symptoms of Koch-Week's conjunctivitis, and 10 of diplobacillary conjunctivitis. The ages of the 24 cases ranged from infancy to 57 years. As the symptoms may resemble those of diplobacillary or Koch-Week's con-

junctivitis, there are no clinical characters by means of which it is possible to make a diagnosis of the presence of the pneumococcus. It is possible that some, perhaps all, were due to Koch-Week's bacillus or the diplobacillus. In some of the proved Koch-Week's and diplobacillary cases a diplococcus was found. In 13 of the 24 cases, in which diplococci only were found, no film was taken.

The diplococcus, which we have presumed to be the pneumococcus, presented the following characters :—

(1) It exhibited a capsule in the films.

(2) On ovarian agar elevated dewdrop-like colonies were found, much larger than the Koch-Week's colonies, and, as a rule, larger than the streptococcus pyogenes colonies. Films made from such colonies showed a diplococcus staining by Gram, and with but little tendency to form chains. The virulence was tested in several cases, but the results were not constant. Mice were inoculated in a few cases with emulsions from the growth after an incubation of 48 hours. The animals did not always succumb. In fatal cases a capsuled diplococcus has been demonstrated in the organs. Diplo-streptococci have been met with in association with the staphylococcus pyogenes, the diplobacillus and Koch-Week's bacilli ; such diplo-streptococci have not been regarded as pneumococci. During the investigation 34 cases of lachrymal obstruction were examined ; in 25 of those a diplococcus similar to that already described was found. Inoculations on mice were made in 18 of the cases in which the diplococcus was found. In the majority a fatal result ensued. In those that died capsuled diplococci were present, but not invariably, in the heart's blood and spleen. The virulence of the cultures varied greatly, and the results were so inconstant that the identification of the pneumococcus by its pathogenic effect on mice was extremely unreliable.

Trachoma has not been met with in this inquiry.

Country Cases.—In the series of 820 cases, 75 came from districts outside the Aberdeen town boundary. In these

cases a distinction has been made, as far as possible, between those living in rural districts and those living in large villages or small towns. Of the 75 cases, two were proved to be due to Koch-Week's bacillus, and two to both Koch-Week's and the diplobacillus. The latter came from places quite near Aberdeen, and connected with it by tramway, car, and suburban railway trains. One of the former came from a large fishing village, the other from a town of more than 12,000 inhabitants. There is reason for believing that the infection by Koch-Week's bacillus in this last case occurred during her stay in Aberdeen, where she had been for some time before coming to the hospital. In the remaining 71 cases micro-organisms were found, as indicated in this table :—

	Cases.
Diplobacillus	37
Gonococcus	1
Pneumococcus	4
"Other forms"...	27
Tubercle bacillus	1
Nil	1

Thirty-six of the 71 cases came from rural districts, and none of these proved to be Koch-Week's cases.

To increase this limited number of country cases, others obtained from various sources have been added, thus, nine are from the cases examined in 1904; 94 cases in all had then to be considered. The age of 20 of these was under 20. In 44 of the cases the diplobacillus was found. The variety and relative frequency of organisms in the 94 country cases is represented thus :—

	Cases.
Diplobacillus	44
Gonococcus	1
Pneumococcus	6
Tubercle bacillus	1
Koch-Week's bacillus	2
Koch-Week's and diplobacillus	2
Nil	2

"Other forms" (staphyloccocus pyogenes, xerosis bacillus, streptococcus pyogenes, pseudodiphtheria bacillus) were found in the remaining cases.

In none of the 41 cases which came from rural districts were Koch-Week's bacilli found.

Early in this inquiry the absence of Koch-Week's cases from the country was noticed. It was thought that the relatively short duration of this form of conjunctivitis might partly account for their absence. In an endeavour to obtain information as to whether Koch-Week's conjunctivitis was scarce in the country, a number of medical friends in rural districts were asked as to their experience of conjunctivitis cases, and slides were sent to at least 22 of them, with a request for a film from any such case coming under their notice. Some of these slides were sent early in February, 1905. It it significant that only 18 slides were returned by the end of the year. On examination they were found to contain once Koch-Week's bacillus, thrice the diplobacillus, once the gonococcus, twice pneumococcus, twice nothing was found in the film; in the remainder only xerosis and staphylococcus pyogenes were discovered. One medical man from a rural district reported that cases of conjunctivitis were very scarce with him. Another reported, six months ago, that such cases were very scarce, and that he would be sure to send a specimen of the discharge if he got such a case. No film has yet been received from him. Another reported that he rarely if ever saw conjunctivitis in country cases. Another, five months after receiving a slide, reported that he had not yet had a case. Another wrote in July, 1905, that he had none of these cases just now. He referred to epidemics of conjunctivitis in which a number of people were infected by one another. "I will, however, send on anything that I can pick up." No slide has been received by 26th March, 1906. Another wrote, "It is a disease I very rarely see." Another wrote, "Conjunctivitis seems to be conspicuous by its absence here." Such statements as these have been made by the majority of country practitioners to whom we have

mentioned the matter. There is evidence therefore to show that the absence, in our series, of cases of Koch-Week's conjunctivitis from rural districts is at least partly accounted for by the rarity of their occurrence in these localities. There is little doubt that numbers of cases of diplobacillary conjunctivitis in the country never seek advice; this is less likely to occur in Koch-Week's conjunctivitis, which is usually a more acute inflammation. In this connection the following experiments are of interest as showing the greater vitality of the diplobacillus than of the Koch-Week's bacillus, when removed from the conjunctival sac; this may explain the comparative rarity of cases of Koch-Week's conjunctivitis in rural districts.

Erdmann* showed that when the discharge of diplobacillary conjunctivitis is placed on linen and exposed to room temperature, the bacillus can remain alive for as long as 14 days. In the few similar experiments made by us the organism was cultivated after four days. This is in marked contrast to the behaviour of Koch-Week's bacilli under the same conditions.

Seasonal Prevalence of Conjunctivitis.—When all town cases of conjunctivitis which occurred during the years 1899 to 1905 are tabulated, in accordance with the dates at which they came for treatment, and arranged in a monthly chart, it is seen that, apart from the constant fluctuation in numbers, there is, in five of the seven years, a distinct spring and autumn rise.

With regard to the form or forms of conjunctivitis which are responsible for this seasonal prevalence, information is only available from the cases, taken consecutively, in 1905. In that year the first rise occurred in March, the second in August, with an intermission in September, succeeded in October and November by the highest rise of the year.

The accompanying chart shows the monthly variation during the year 1905 in the number of cases of (1) all forms

* Ein Beitrag zur Kenntniss der Diplobacillen Geschwür, Klinische Monatsblätter für Augenheilkunde, May, 1905, p. 561.

of conjunctivitis; (2) diplobacillary conjunctivitis; (3) Koch-Week's conjunctivitis; (4) conjunctivitis associated with the pneumococcus; (5) gonorrhœal conjunctivitis; (6) other varieties of conjunctivitis.

The Spring rise is seen to be caused by an increase in the number of cases of conjunctivitis due to the diplobacillus, Koch-Week's, and "other forms," the greatest increase being in the diplobacillary cases.

The August rise is due to the Koch-Week's bacillus and diplobacillus, chiefly the latter.

The October-November rise is caused in the former month by an increase of the Koch-Week's bacillus, the diplobacillus, and "other forms"; in the latter month, during which the numbers still further increased, the Koch-Week's bacillus was wholly responsible. Saemisch* states that epidemics of Koch-Week's conjunctivitis are most frequent during the summer. Gonin† says that diplobacillary conjunctivitis is most frequent during hot, dusty summers.

In seeking to explain seasonal variations, the weather reports for the City of Aberdeen were consulted as to rainfall, wind, and temperature.

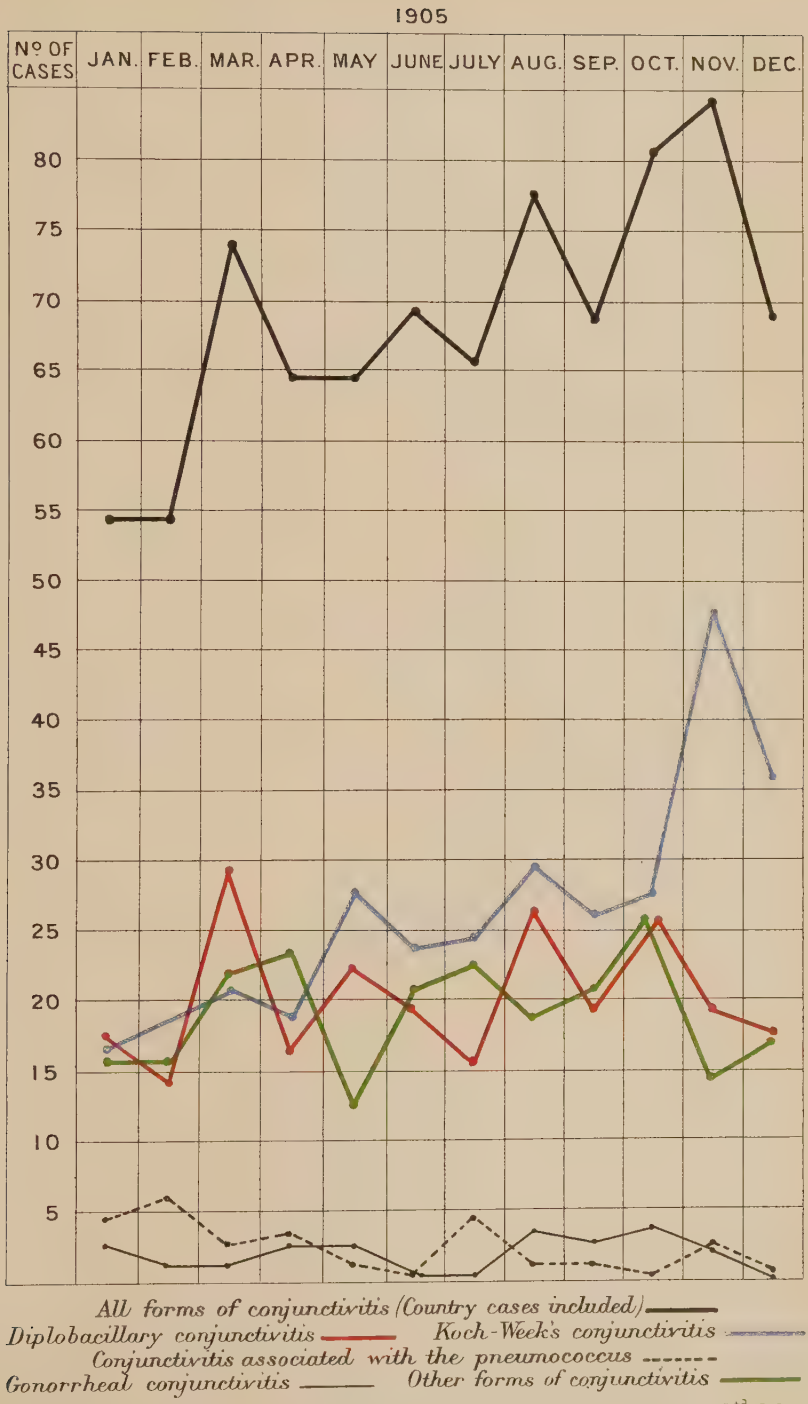
Rainfall: As a relationship between rainfall and the prevalence of conjunctivitis seemed to exist, the total rainfall for each year was taken; the total rainfall for each month was then taken and the percentage reckoned for each month with reference to its corresponding year. In 54 of the 84 months the amount of rainfall is in inverse proportion to the number of cases, *i.e.*, the greater the rainfall the fewer are the cases of conjunctivitis, and *vice versâ*.

The cases compared in the same way with reference to wind and temperature showed no evident connection.

Charts were prepared showing for each week in 1905 the number of cases of all forms of conjunctivitis, also of Koch-Week's cases by themselves, similarly diplobacillary and "other forms"; when these were compared with the weekly

* Graefe-Saemisch Handbuch, 2 aufl., article by Saemisch, p. 32.

† Graefe-Saemisch Handbuch, 2 aufl., article by Saemisch, p. 47.



Bale & Danielsson, Ltd. lith.

rainfall, temperature, and velocity of wind, no apparent connection could be established.

Conclusions.—As the result of this examination of a series of consecutive conjunctivitis cases, extending over a complete year, it is shown that the great majority of cases of conjunctivitis in this locality are due to the Koch-Week's bacillus and the diplobacillus of Morax-Axenfeld, the former predominating, although not largely.

The number of cases in which Koch-Week's bacillus was found was 310; diplobacillus of Morax-Axenfeld 274; gonococcus, 18; tubercle bacillus, 1; pneumococcus (unassociated with any of these micro-organisms), 24. Of the cases assigned to the group of "other forms," a large number, we believe, were either due to the Koch-Week's bacillus or the diplobacillus, although neither of these organisms was demonstrated.

Of the more important clinical characters by which a differential clinical diagnosis of the Koch-Week's bacillus is made, it was found that *conjunctival hæmorrhages* occurred in only 21·16 per cent. of the cases; that the *age* in 235 of the 284 cases was under 14 years, and that no case of conjunctivitis due to this germ came from a *rural district.*

The Koch-Week's bacillus, which was demonstrated in 310 cases, was associated with the diplobacillus on 36 occasions.

Recurrent attacks of conjunctivitis have been bacteriologically proved to be caused by the Koch-Week's bacillus. An interval elapsing between the attacks as long as 15 months has been noted.

In the majority of all cases due to the Koch-Week's bacillus a correct clinical diagnosis can be made, in this series, 86·4 per cent. Typical cases present no difficulty in diagnosis; on the other hand, there is a small number which are impossible of diagnosis.

Cultures of the Koch-Week's bacillus can be readily obtained when ovarian agar is employed; this medium is

superior to those in which other human body fluids are used.

Citrated ox-blood agar is excellent for the growth of Kock-Week's bacillus, and has the advantages that (a) the colonies are more conspicuous than on ovarian agar, (b) ox-blood can be readily obtained from a slaughter-house.

Of the more important clinical characters by which the diplobacillus can be recognised as the cause of a conjunctivitis, the appearances at the outer or inner canthus which have given rise to the term angular conjunctivitis are almost pathognomonic. Angular conjunctivitis, however, only occurred in 34·7 per cent. of the diplobacillary cases in this series.

Although the majority of diplobacillary cases occur in adults, 28·46 per cent. are met with in patients under 14 years of age.

Bacteriological proof has been obtained of the recurrence of diplobacillary conjunctivitis.

The infectious character of diplobacillary conjunctivitis was shown in instances where several or all of the members of a household were simultaneously affected.

The majority of cases of diplobacillary conjunctivitis came after symptoms had been present for a longer interval than in the case of those affected with the Koch-Week's bacillus; of the former, 164 cases came after an interval of at least two weeks—many after a much longer interval—and of the latter, 242 cases came after an average interval of 6·8 days. In diplobacillary cases the interval since onset of symptoms in children is shorter than in adults.

A correct clinical diagnosis of the diplobacillus can in the majority of cases be made, in this series 72·4 per cent.

Cultures of the diplobacillus are obtained without difficulty on ovarian agar.

The gonococcus can be readily grown on ovarian agar.

The presence of the pneumococcus in a case of conjunctivitis cannot be clinically ascertained.

In infants (one year or less) the commonest form of

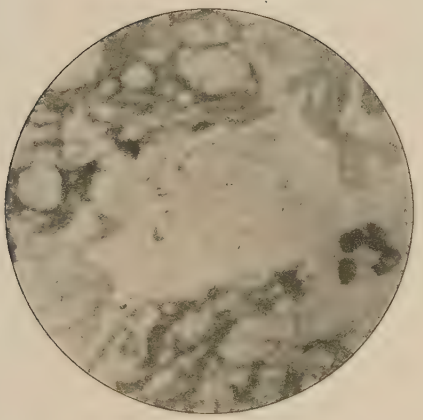


FIG. 1. Koch-Week's bacilli in conjunctival discharge. × 820.

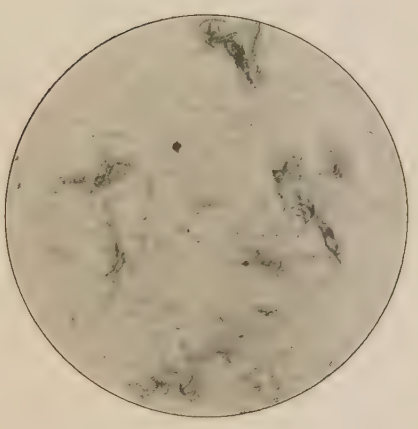


FIG. 2. Koch-Week's bacilli. Involution forms from a 96 hours' culture on ovarian agar. × 820.

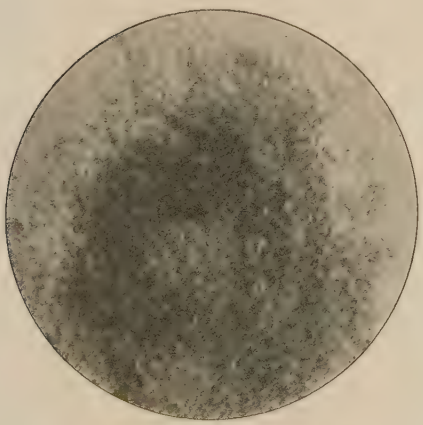


FIG. 3. Koch-Week's bacilli. Impression preparation of a colony from a 24 hours' culture on ovarian agar. × 820.

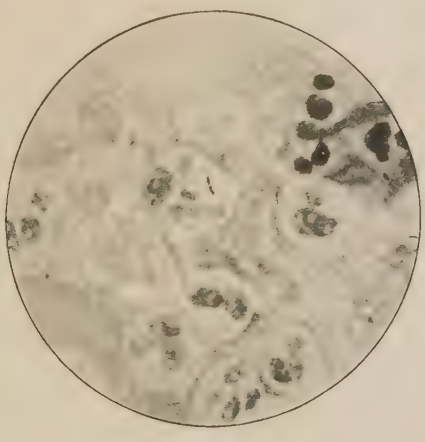


FIG. 4. Koch-Week's bacillus, with the diplobacillus in conjunctival discharge. Mixed infection. × 820.

Bale & Danielsson Ltd.

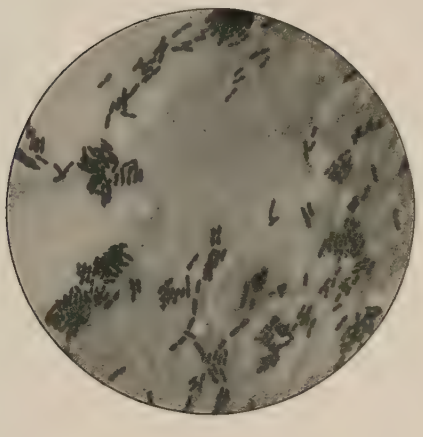


FIG. 5. Diplobacilli in conjunctival discharge. × 820.

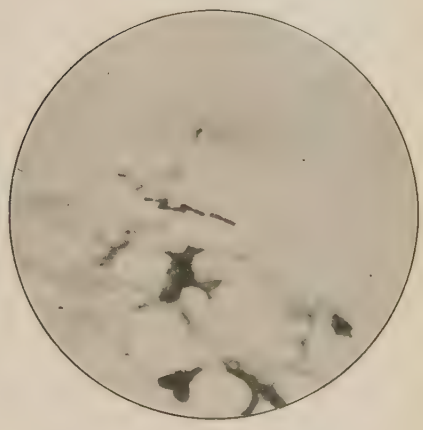


FIG. 6. Diplobacilli (long form) in conjunctival discharge. × 820.

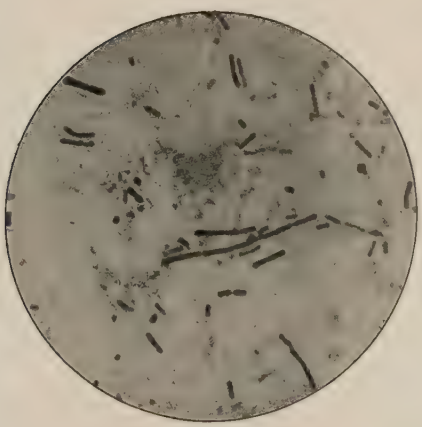


FIG. 7. Diplobacilli. Involution forms from a 132 hours' culture on ovarian agar. × 820.

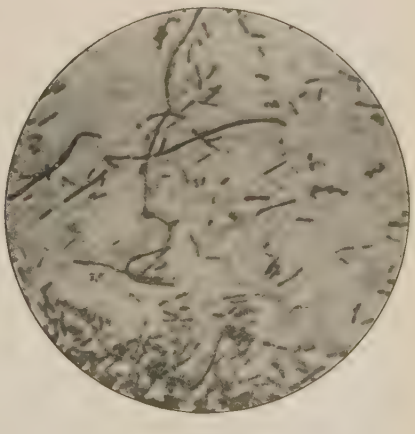


FIG. 8. Diplobacilli. Involution forms from a 132 hours' culture on ovarian agar. × 820.

Hale & Danielsson, Ltd.

conjunctivitis is that due to the Koch-Week's bacillus, the next in order of frequency is the gonococcus, and then the diplobacillus.

No definite relationship has been established between climatic conditions and the prevalence of the various forms of conjunctivitis.

By the kind permission of Professor Hamilton we have carried out the greater part of our bacteriological work in the Pathological Department at Marischal College. To those who have in any way furnished us with material for this investigation we are indebted, more especially to the surgeons of the Aberdeen Royal Infirmary, who have so readily given us every facility for obtaining the various fluids required.

RING SCOTOMA.

By W. Ilbert Hancock.

The subject of ring scotoma though not even mentioned in the majority of our text books is one of great interest, and its careful study, together with a faithful record of cases, might not improbably add much to our present knowledge of the distribution of the optic nerve fibres. Although there are a considerable number of recorded cases in ophthalmic literature, but few attempts have been made to deal exhaustively with the subject. Many theories have been advanced to explain the curious anomaly in the field of vision, and not a little confusion has arisen with regard to the cases which fall within this category.

Some have recorded under the term "ring scotoma" small crescentic defects in the field, others insular scotomata grouped in a more or less circular manner.

Although, no doubt, partial rings are only what one might expect, and are of great importance in the study of this condition, yet at the same time before interpreting such cases due care should be exercised in excluding the possibility of their being accidental occurrences.

With regard to the character of the scotoma, in position it practically always occurs in the intermediate part of the field of vision, the macular region and periphery remaining intact. Its outline, as a rule, is zig-zag, sometimes markedly so, though occasionally both its inner and outer limits may be quite regular.

The density of the scotoma frequently varies in different parts, some portions presenting an absolute, others a relative defect, or again, it may be relative throughout its whole extent.

The following cases have come under my personal observation, and for permission to publish Case 2, I am indebted to Mr. Treacher Collins :—

Case 1.—Miss H., age 26, consulted me in November, 1904, complaining of defective sight in her left eye, and gave the following history:—

In August, 1902, whilst fastening the window in her bedroom during an exceptionally heavy thunderstorm she was, as she expressed it, "Struck and rendered unconscious by an extremely vivid flash of lightning which appeared to strike the left side of my face." The patient remembers nothing more until finding herself in bed some hours later.

Her friend, in whose house she was staying at the time, in reply to a communication from me, has favoured me with the following narrative:—

"Whilst sitting in the dining room of the ground floor I was startled by a loud scream from Miss H. in the room above, and on rushing upstairs found her unconscious on the floor. We put her to bed and applied hot bottles and restoratives, but it was quite an hour before she showed signs of returning consciousness. On recovery Miss H. complained that she was quite blind in both eyes, but thinking this was the result of the shock we thought little of it and no medical man was summoned."

On the following morning both eyes were much inflamed and the lids swollen, and though the sight in the right eye had quite returned the left was still blind. At the end of 48 hours the vision in the left eye commenced gradually to return, the improvement continuing for about 10 days, by which time the sight was as good as it has ever been since the accident.

There was no burning of the face, eyelashes or eyebrows.

On her visit to me, in November, she complained that on looking at an object with the left eye, the right eye being covered, it appeared to be surrounded by a circular shadow, which was constantly present and was darker in some parts than in others. Examination of the pupils showed the right to have a brisk normal reaction. The left contracted well to light, but the contraction was distinctly less well maintained than in the fellow eye, and after several oscillating movements the pupil came to rest slightly larger than the right.

$$V\begin{cases}\text{R.} & \bar{c} + 1 \text{ Dsph.} + \cdot 5 \text{ D}\downarrow = 6/4, \text{ J}_1 \\ \text{L.} & \bar{c} + 1 \text{ Dsph.} + \cdot 5 \text{ D}\downarrow = 6/6 \text{ partly, J}_1\end{cases}$$

The media and fundi in both eyes were perfectly normal.

A very careful examination of the affected eye under a mydriatic failed to demonstrate anything abnormal, *e.g.*, pigmentary disturbance or evidence of old neuritis.

Light sense tested with Bjerrum types.

R. $\bar{c}$ correction = 6/6.

L. $\bar{c}$ „ = 6/60 barely.

No history of night-blindness either before or after the accident.

Fields of Vision.—Right perfectly normal to both white and colours.

Left. Shown, Fig. 1.

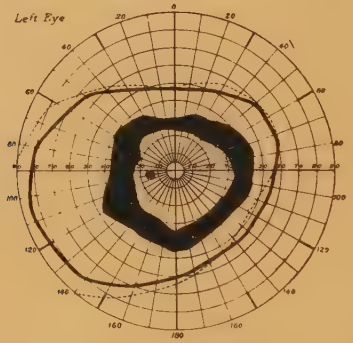


Fig. 1.—The ring scotoma was not so sharply defined as shown above, but was fringed by an area a few degrees in extent, in which there was a relative defect impossible to map out accurately. The colour fields compared with the fellow eye were markedly contracted.

The above field was taken on three different occasions at intervals of about a month and proved to be practically the same on each visit.

With regard to her family history her mother and father are living and well. She has two sisters and two brothers quite healthy, but one of the former suffered from chorea at nine years of age.

The patient was undoubtedly a girl of the neurotic type, but a careful examination of her nervous system failed to reveal anything abnormal, and I may add that she has never had an attack of unconsciousness before or since. I

at first thought that I was dealing with a functional disturbance, but the presence of a ring scotoma, involving a precisely similar portion of the field when taken on three different occasions after considerable intervals of time, the reaction of the pupil, and the defective light sense, point beyond doubt to there being some organic mischief.

Case 2.

Henry H., age 46, was first seen on September 27, 1903. He complained that the sight in the right eye commenced to fail about six weeks before, and since that time had gradually become worse. He was suffering from frontal headache and had completely lost his sense of smell.

No specific history; moderate smoker. Nervous system normal.

V. { R. Hand movements; not improved.
L. $\bar{c} + 1{\cdot}5 = 6/6\ \bar{c} + 2{\cdot}5 = J_1$.

R. Pupil inactive to light or accommodation.

L. Pupil briskly active to both.

No pain on pressure on globe or in extreme movements.

R. Very little ophthalmoscopic change, but optic disc perhaps a little paler and more homogenous looking than the L.

L. Fundus and media normal.

Fields of Vision.

R. Large central scotoma peripheral field normal.

L. Normal.

Patient was treated with blisters to the right temple and potassium iodide internally, and the sight rapidly commenced to improve but never quite recovered.

On February 15, 1904, he again visited the Hospital.

V. { R. $\bar{c} + 1{\cdot}5$ Dsph. $= 6/9$ letters $\bar{c} + 2{\cdot}5 = J_1$.
L. $\bar{c} + 1{\cdot}5$ Dsph. $= 6/6\ \bar{c} + 2{\cdot}5 = J_1$.

R. disc very pale, especially in temporal half, macula normal.

L. Fundus and media normal.

Field of Vision.

L. Normal.

R. (See Chart, Fig. 2.)

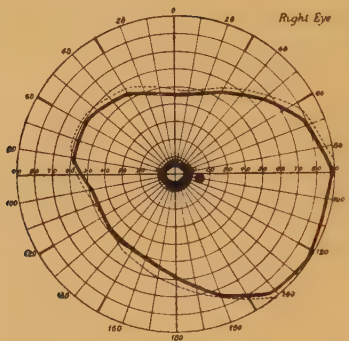


FIG. 2.—Peripheral field normal. A relative ring scotoma very definitely made out immediately surrounding the fixation point, roughly between the 3° and 10° circles.

CASE 3.

David H., age 28, came to the Hospital complaining of night-blindness. This trouble was first noticed eight years before, but

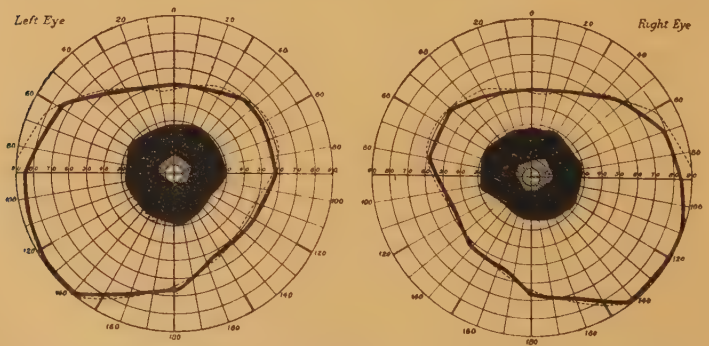


FIG. 3.—R. and L. fields taken with a 10 mm. white object, showing absolute ring scotoma between the 10° and 30° circles.

had become considerably worse during the last two years. He has one brother living, similarly affected, one sister, aged 20,

unaffected. An elder brother, who is dead, also suffered from night-blindness. Father and mother both died when patient was quite young, and he did not know if there was any blood relationship between them.

V. { R. = 3/60, J 20 not improved.
L. = 6/60, J 12 not improved.

Fields of Vision.—(See Fig. 3.) R. and L. Fundi almost identically the same. Retinal arteries very contracted, discs waxy ; some sclerosis of choroidal vessels. Very marked "pepper and salt" fundus throughout with a very few small areas of branching retinal pigmentation in the extreme periphery.

Very marked granular appearance at each macula.

The case was in fact typical of the condition known as retinitis pigmentosa sine pigmento.

Many theories have been advanced to explain the ring-shaped defect in the field, some accounting for individual cases, others attempting to explain one and all by the same hypothesis. Of these we have the following :—

A. Which attributes the scotoma to a lesion of the retinal vessels and accounts for its ring-like character by the arched course of these vessels around the macula. (Hersing, Bull.)

B. Asserts that, owing to the anatomical arrangement of the venæ vorticosæ, the choroid at the equator of the eye-ball is more richly supplied with blood than other parts, and therefore more likely to become diseased. (Schön.)

C. Explains the scotoma as being the result of an exudation. The characteristic form is accounted for by assuming that the tension of the choroid and retina is less in the equatorial than in the antero-posterior direction, and therefore it is in the former direction that any exudation from the choroid would extend, and thus give rise to a circular defect in the field of vision. (Crzellitzer, Wettendorfer.)

D. Claims that ring scotoma is but the expression of impaired function of the retinal rods and can be demon-

strated in every case of night-blindness irrespective of causation. (Heinrichdorf.)

E. The equatorial belt of the fundus being situated at the point of meeting of the anterior and posterior ciliary system is not so well supplied as other parts of the eye. In fact, as Nettleship tersely expresses it, "the equator seems to be a sort of 'divide' between the two systems and to be not very efficiently served by either, whilst the current must be slowed or reversed in many of the anastomosing twigs. Given a congenital tendency (as in retinitis pigmentosa) to atrophy or hardening of the inner layers of the choroid it would probably tell first where the nutrient stream is weakest." (Gonin, Nettleship.)

F. That the cases are best explained by a retro-ocular lesion of the optic nerve. (v. Graefe, Leber, Burnett, Gallus.)

Of these theories the first three have so many obvious objections, and have already suffered so severely at the hands of their critics, that a further discussion of them is hardly necessary.

Ring scotoma has been met with in the following conditions:—

(1) Retinitis pigmentosa (including retinitis pigmentosa sine pigmento).
(2) Retinitis, choroiditis, and retino-choroiditis.
(3) Lesion of the optic nerve with or without optic neuritis.
(4) Glaucoma.
(5) Idiopathic night-blindness.
(6) Myopia.

Let us then consider these groups of cases in the above-mentioned order:—

(1) *Retinitis pigmentosa.*—It is in this affection that this form of scotoma most frequently occurs, and, indeed, it

seems highly probable that in the majority, if not in all, cases, it is one of the earliest manifestations of the disease. The scotoma is always progressive and has no definite relationship to the area of most marked pigmentation.

The vascular theory of Gonin and Nettleship was ingeniously devised to explain such cases, and was no doubt prompted by the fact that the scotoma occurs not infrequently in that part of the field which would roughly correspond to the equator.

The chief objections to the above theory are, in my opinion—

Firstly, that there are cases of retinitis pigmentosa in which the extreme outer limit of the ring scotoma in parts does not extend beyond the 15° circle (see Fig. 4).

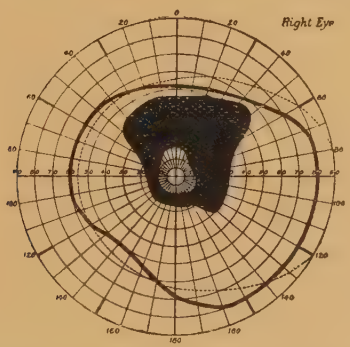


Fig. 4.—Field of vision from a case of retinitis pigmentosa (Gonin, Annales d'Oculistique, vol. cxxv, 1901).

Now, it has been proved by Hallidie and others that the equator of the eyeball is situated 67° from the fixation point. We have, therefore, a considerable distance between the extreme outer limit of a portion of the scotoma in Fig. 4 and the equator.

Again, in Case 3, in no part does the scotoma extend beyond 30°.

Gonin explains the varying position of the scotomata in the following way:—

"If the sclerosis of the choroidal arteries attacks simultaneously the anterior and posterior systems, it is in the intermediary zone at the equator that the scotoma will be situated. If, on the other hand, the posterior system is the first attacked, or, on the contrary, it is less severely attacked than the recurrent branches, then the scotoma will be situated more centrally in the former case, or more peripherally in the latter."

Even if we admit the "divide" to be comparatively broad and also admit that its anatomical position may be open to slight variation, yet it seems impossible to account for the position, assuming, as he does, that in such cases it is the terminal twigs of the posterior ciliary arteries that are first affected.

Secondly, the outline in a number of the scotomata in retinitis pigmentosa is perfectly regular, and it is hardly conceivable that a degenerative condition affecting a complex vascular network could spread in such a perfectly even manner.

Thirdly, the 15 to 20 ciliary arteries perforate the globe in a circle round the optic nerve, yet in all the cases pictured it is strikingly evident that the scotoma is concentric with the point of fixation, not with the blind spot.

(2) *Retinitis, Choroiditis, Retino-Choroiditis.* — It is a striking fact that certainly in many cases of ring scotoma occurring in the above conditions, the defect in the field of vision does not correspond to the part of the fundus seen ophthalmoscopically to be diseased.

Again, the scotoma may vary considerably without a variation in the ophthalmoscopic picture, and in other cases it has disappeared, in spite of the fundus disease being of a progressive character. (Gallus.)

In almost all there has been a definite specific history, in fact some authors have stated that a ring scotoma occurring in retino-choroiditis is pathognomonic of syphilitic disease. Nettleship explains the ring scotoma in this group of cases by assuming arteritis of the equatorial twigs of the choroidal

arteries, either of the posterior or anterior system, or both. This explanation is not satisfactory for all cases, notably one of syphilitic retinitis comparatively recently described by Handmann.

Female, age 45.—Specific history. No night-blindness.

V { R. = 6/9.
  { L. = 6/6.

R. Circular area of retinal pigmentation, including disc and macula within it. It approaches closely to the disc on the nasal side and almost touches the macula on the temporal. Disc somewhat blurred in temporal half, good colour. Arteries slightly narrowed. Periphery of fundus normal. Field shows a ring scotoma concentric to the fixation point and lying entirely between the 5° and 30° circles. Field for white normal.

L. Fundus change much the same as right, but pigmentation not nearly so pronounced, and its ring-like distribution incomplete, being most marked on nasal side of disc, less marked on the temporal side and absent above and below. Arteries and disc normal. Field shows a crescentic absolute scotoma, situated roughly between 10° and 20° around the upper half of fixation point. Peripheral field taken in a dull light quite normal.

Here we have a case in which the outer limit of the scotoma does not extend beyond the 30° circle, and cannot be explained by assuming an arteritis of the "equatorial twigs."

This is also an interesting case as being one of the instances in which the defect in the field corresponds fairly accurately in the right eye with the diseased area in the fundus, but it will be noticed that there is no such correspondence in the left eye.

(3) *Lesions of the Optic Nerve with or without Optic Neuritis.*—There are cases recorded of ring scotoma in which the fundus has been perfectly normal, and which clinically were typical of the class known as retrobulbar neuritis. Burnett, many years ago, described a most interesting case which is extremely difficult to explain by any other hypothesis than a tract or chiasma lesion.

Male, age 55.—Syphilis two years before his first visit. A year before had an attack of inflammation in both eyes with acute pain.

V { R. = 4/30 not improved.
L. = 4/30 „

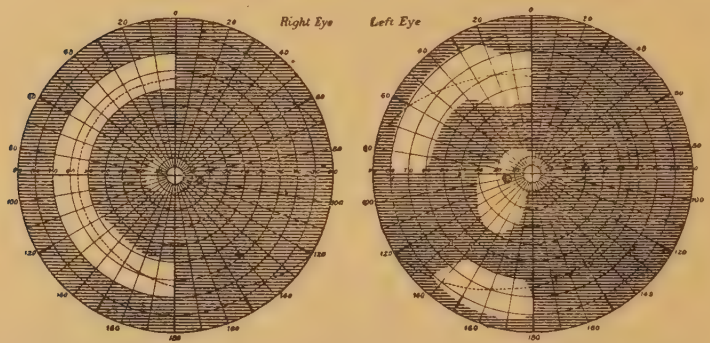


FIG. 5.—Burnett's case. Fields of vision taken on first visit of the patient, showing hemianopia and presence of a ring scotoma in retained half of the field (Trans. Amer. Ophth. Soc., 1887).

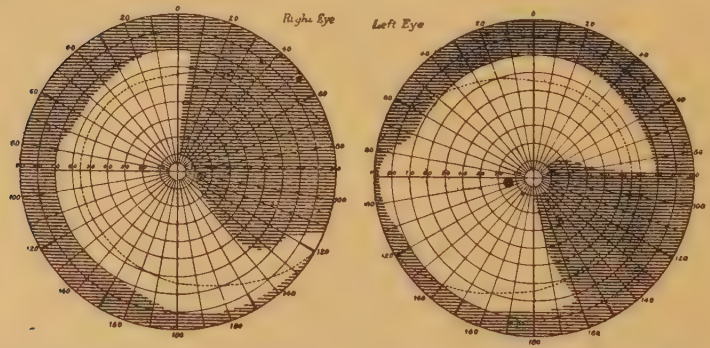


FIG. 6.—Fields taken a month later. The ring scotoma has entirely disappeared and there is a partial recovery of the hemianopic field.

R. and L.—Some posterior synechiæ with spots of pigment on lens capsule. Fine vitreous opacities. No choroiditis. Retinal vessels normal. Fields (Figs. 5 and 6). Patient treated by inunction of mercury.

A fortnight later severe headache and numbness on left side

of body: Vitreous clearer. Fundus normal. Eight months later V. R. and L. = 4/15. Vitreous clearer.

The patient was watched for nearly two years, the fields showing varying forms, the vision greatly improving. When last seen the left field was practically normal, and the right showed some irregular peripheral contraction with two small insular scotomata. A note of the fundus at this time says there was some disturbance of pigmentation down and out in right, reaching nearly up to the macula. In left—patch of pigmentary change up and out six to eight disc diameters from nerve head.

Evidently there was here a complete loss of function of the left tract with, at the same time, implication of the intermediate fibres in the right.

The dividing line between the two halves of the field of vision is typical of hemianopia, namely, strictly vertical with a reëntrant angle at the point of fixation, leaving central vision intact. Lastly, we have the changing forms in the field, which could only be explained by a varying pressure on the tracts or chiasma.

It might possibly be argued that in the above case the hemianopia was due to a tract lesion, and the ring scotoma to a retinitis.

Against this, however, it is extremely unlikely that a retinitis could cause such a perfectly regular circular scotoma as was present in the right eye.

Burnett, in his communication, directs attention to Bunge's assertion that the macular bundle supplies the central area of the retina for an oval space of approximately 20° in the horizontal and 10° in the vertical direction. He further points out that in the two cases recorded by him the area of central vision remaining unaffected is almost the exact counterpart of the central scotoma met with in circumscribed retrobulbar neuritis.

A case not unlike the above has been recorded by de Schweinitz:—

The visual fields in this case were taken at irregular intervals over a period of five years. When first seen, there

was an absolute scotoma in the left lower quadrant of each eye. Four years later the fields showed in addition to the previous lesion a typical right lateral hemianopia. Five years after the first visit the large defects in the fields had cleared up, and there was now present a slight peripheral contraction, and a ring scotoma in each eye, roughly between the 10° and 30° circle.

The fundi were perfectly normal throughout.

From our present incomplete knowledge of the distribution of the optic nerve fibres it is extremely difficult, if not impossible, to explain how the annular scotoma is brought about in retro-bulbar neuritis, using the term in its broadest sense. A careful study of the most recent experimental work on the subject by Usher and Dean, and by Parsons, shows that we only know of one specialised bundle in the optic nerve, namely, that composed of the fibres supplying the macula. Yet the remaining fibres of the nerve have a fairly definite arrangement, and it is generally accepted that those most peripherally situated supply the intermediate portion of the retina, and those more centrally placed are distributed to the peripheral retina. This arrangement is fairly constant throughout the whole length of the optic nerve, modified only by the varying position of the macular bundle which, as is well known, occupies a wedge-shaped area at the temporal side of the disc, and gradually takes up a central position in the nerve before reaching the bony optic foramen.

A lesion, therefore, destroying the peripheral fibres of the optic nerve would give rise to a defect in the intermediate field arranged in a circular manner.

Gallus, in advocating the retrobulbar origin of this form of scotoma, puts forward a new theory of the pathology of retinitis pigmentosa.

He assumes that the primary cause is compression of the optic nerve and ophthalmic artery at the bony optic canal from chronic periostitis. At this point the macular bundle is centrally situated, and the fibres of the optic nerve, which

are here peripheral, are distributed to the intermediate portion of the retina.

The first effect, therefore, of the pressure is to destroy the function of the most superficial fibres which gives rise to a ring scotoma.

The narrowing of the retinal vessels he explains by a like compression of the ophthalmic artery. If the pressure is continued a gradually increasing atrophy of the nerve takes place with a corresponding peripheral contraction of the field of vision, the macular bundle being here centrally placed is therefore the last to suffer.

Lastly, he explains the retinal pigmentation so characteristic of the disease as resulting from the degeneration and thickening of the ciliary arteries, which he asserts is the necessary concomitant of long-continued pressure on their parent trunk. This theory is unsupported by any pathological data, and his deductions as to the effect on the retinal and ciliary vessels of compression on the ophthalmic artery seem to me unsatisfactory.

(4) *Glaucoma.*—It would appear, from the paucity of cases recorded, that ring scotoma occurs very rarely in glaucoma, and, as far as I have been able to ascertain, there are only 7 cases mentioned in ophthalmic literature (Noyes, Mittendorf, Handmann, de Schweinitz, Zentmayer and Posey, Pflüger, Bjerrum).

Of these, Handmann's is the most recently described:—

Female, age 59. Sought advice for a "shadow" in the right eye.

R. $\bar{c}$ correction = 6/6, J_1 T*n*.

L. $\bar{c}$ correction = 6/6, J_1 T*n*.

R. Shallow anterior chamber. Very marked pathological cupping of disc, with some pallor.

L. Shallow anterior chamber. Pathological cupping of disc, but not so extensive as in fellow eye. Nerve good colour.

R. Field showed a ring scotoma between the 10° and 20° circles with some concentric contraction in the field for white.

L. Field normal.

Several suggestions have been made to explain the scotoma in this disease. Thus it has been attributed to a mere accidental occurrence, to an invisible affection of the rods and cones, and lastly by Bjerrum to the destruction of the fibres in the papilla at the margin or sides of the excavation.

The loss of field in glaucoma is the result of pressure either on the nerve fibres or retinal vessels, or both; and compression of the nerve fibres against the unyielding scleral canal implicating only those most peripherally placed at the disc, might possibly explain a case such as Handmann's.

The recorded cases are so few that it makes it extremely difficult to offer a satisfactory explanation, and it is quite possible that if the fields of vision in cases of glaucoma were more systematically searched within their boundaries with a small test object, ring scotoma would be more frequently found in this condition.

With this object in view, Bjerrum's method of testing the field of vision would, no doubt, be an admirable one. Unfortunately, however, the length of time required to carry it out satisfactorily renders it, at least in hospital work, quite impracticable.

(5) *Idiopathic Night-blindness.* — Heinrichdorf, in his recently published paper, after accepting as proved that the rods are the basis of vision of low intensity, gives the fields of 11 cases which he has examined. Retinitis pigmentosa (6), retinitis pigmentosa sine pigmento (1), idiopathic night-blindness (1), monocular optic neuritis (1), neuro-retino-choroiditis (1), disseminated choroiditis with retinitis pigmentosa (1).

He shows that in some of these cases the field of vision was perfectly normal when taken in a bright light, but when taken with a dull illumination there was present a well-marked complete or partial ring scotoma. He argues that in all cases of night-blindness, whether congenital or acquired, a ring scotoma can be demonstrated if the field of vision be taken in a dull light. Unfortunately, the

descriptions of his cases are meagre, practically confined to vision and diagnosis, and he gives no explanation of why the scotoma should take this form. It is therefore difficult to judge of the value of this communication.

(6) *Myopia.*—With regard to the ring scotoma occurring in the above condition, I can find but few references to the subject.

Weiss has described cases of both relative and absolute ring-shaped defects which he ascribes to extension of the blind spot above and below; the prolongations occasionally pass in a crescentic manner temporalwards, and meeting to the outer side of the fixation point enclose the latter within the circle.

Wettendorfer, in a lengthy communication, arrives at the following conclusions:—

(1) In the majority if not in all cases of myopia above 6 D, if the field is mapped out carefully with a 5 mm. object in a good light, there will be found concentric zones in which there is either a relative or absolute scotoma.

(2) The scotoma is always negative.

(3) The commonest situations are—

(*a*) Prolongation of the blind spot.

(*b*) In the periphery, leaving only a narrow belt a few degrees in extent between it and the extreme peripheral limits of the field of vision.

Between these two situations not infrequently other concentric scotomata may be mapped out so that there may be as many as five rings, the field resembling a target.

(4) The abnormalities of the field are entirely independent of changes in the fundi, and the greatest precautions were taken to guard against the scotomata being due to fatigue.

So far as I know, these results have not been verified by any other observers, and one must hesitate before accepting them.

Of the three cases described by me at the commencement of this paper, Case 1 is of great interest, from a speculative point of view, not only as to the site of the lesion, but also as to its causation.

Lightning injuries of the eye are but seldom met with in this country, and with regard to the *modus operandi* of the electric energy, Collins, in a communication in the Trans. Ophth. Soc., suggests that it may act in one or more of three different ways:—

(1) By the heat rays producing, *e.g.*, burns of the lids and conjunctiva.

(2) By the chemical ultra-violet rays giving rise to symptoms similar to those met with in snow-blindness and ophthalmia electrica, *e.g.*, blepharospasm, conjunctival hyperæmia.

(3) By electrolytic action or concussion giving rise to changes which can be reproduced on animals by shocks from Leyden jar batteries, *e.g.*, paralysis of ocular muscles, retinal hæmorrhages, optic atrophy, ruptured choroid, and detached retina.

There can, I think, be no doubt that the organic mischief in the above case was brought about by the lightning, and from the entire absence of ophthalmoscopic fundus disease it is fair to assume that the site of the lesion was probably in the optic nerve. On the other hand, it must be remembered that Birch-Hirschfeld has shown that the ultra-violet rays have a marked effect on the ganglion cells of the retina, which at once suggests the possibility of there being a primary retinal lesion; but even accepting this as a possibility, we have still to account for its circular distribution—an insurmountable difficulty.

Case 2 is of unusual interest from the position of the

scotoma, which apparently involves part of the macular bundle, and it seems to me that the most probable explanation is that it is due to a clearing up of the mesial area alone of the large central scotoma, which was a prominent feature on the first visit of the patient.

CASE 3 is described to show that the ring scotoma in retinitis pigmentosa does not always correspond to the equator.

To summarise this communication: If we exclude the very rare cases of glaucoma, idiopathic night-blindness, and myopia as requiring further verification, the cases fall into two main groups.

A. Those cases in which the retina or choroid is diseased:—

(1) Those in which the diseased area of the fundus corresponds with the scotoma in the field.
(2) Those in which there is no such correspondence.

B. Those cases in which the fundus to ophthalmoscopic examination is perfectly normal.

These groups of cases are explained by two separate hypotheses. The one invokes an *intra*-ocular, the other an *extra*-ocular causation. Those who favour the former explain the scotoma in retinitis pigmentosa upon the generally accepted pathology of that disease, viz., that the primary lesion is a sclerosis of the choroidal vessels, and account for the ring by the Gonin-Nettleship hypothesis. In the cases of retino-choroiditis a similar interpretation is given, but no attempt is made to explain cases in which the fundus disease does not correspond to the position of the scotoma.

Lastly, those cases in which the fundus is perfectly normal are either ignored or dismissed by assuming that there is an invisible lesion of the sentient retinal layer, which to my mind is quite inadmissible.

With regard to the second hypothesis (the extra-ocular

causation), the fact that we have a definite group of cases of undoubted retrobulbar neuritis with ring scotoma, but without fundus change, is to me positive proof that a pure nerve lesion will account for this ring-like defect in the field of vision, and the peculiar correlation of groups of fibres in the optic nerve with concentric areas in the retina gives a reasonable confirmation of this view.

This retrobulbar view could also be applied to those cases of ring scotoma in retino-choroiditis where the defect in the field does not correspond with the area of fundus change, and it is strongly supported by the cases of Burnett and de Schweinitz with hemianopia.

In retinitis pigmentosa I have shown that to me the Gonin-Nettleship view fails to explain the ring defect in many cases.

Lister, in describing the microscopical appearances of a case of retinitis pigmentosa, after pointing out that there is no sclerosis in the choroidal arteries, says :—

"Some hold that these changes are brought about by primary vascular disease either of the retina or choroid. But the concentric defect corresponds with a *nerve distribution* rather than a *vascular distribution*, and therefore I think we must look for a degeneration commencing primarily in the nervous tissues rather than in either vascular system."

This is perhaps too much to assume till further evidence is at hand, but it receives support from the definite retrobulbar cases with ring scotoma mentioned above.

In conclusion, my best thanks are due to Dr. Markus, to whom I am greatly indebted for helping me with the foreign literature on this subject.

Bibliography.

Baas. Arch. f. Ophth., Bd. xliv. Ophth. Congress zu Heidelberg, 1897.
Baas. Das Gesichtsfeld, 1896.
Bjerrum. 1890. Xth International Congress, p. 66.
Bull. Perimetrie, 1898.
Burnett. Trans. Americ. Ophth. Soc., 1887, p. 449.
Collins. Trans. Ophth. Soc., vol. xxiii, 1903, p. 114.
Crzellitzer. Arch. f. Augen., Bd. xl, p. 279.
De Schweinitz. International Clinics, 4th Series, vol. iii.
Gallus. Zeitschr. f. Augen., 1902, p. 361.
Gonin. Annales d'Oculistique, vol. cxxv, 1901, p. 101.
Hallidie. Roy. Lond. Ophth. Rep., vol. xiv, p. 361.
Handmann. Zeitschr. f. Augen., Bd. vi, 1901, p. 127.
Heinrichdorf. Arch. f. Ophth., Bd. lx, p. 405.
Hersing. Arch. f. Ophth., Bd. xviii, Heft 2, p. 69.
Landolt. Annales d'Oculistique, vol. lxxxiii.
Lister. Roy. Lond. Ophth. Rep., vol. xv, part 3, p. 254, 1903.
Mittendorf. Trans. Americ. Ophth. Soc., 1887, p. 449.
Nettleship. Roy. Lond. Ophth. Rep., vol. xv, part 3, 1903.
Noyes. Trans. Americ. Ophth. Soc., 1889, p. 299.
Parsons. Brain, 1902, part 99.
Pflüger. Ophth. Congress zu Heidelberg, 1885, p. 94.
Schön. Die Lehre von Gesichtsfeld, 1874.
Silex. Zeitschr. f. Augen., 1899, Bd. ii, p. 150.
Uhthoff. Archiv für Psychiatrie, vol. xxi.
Usher and Dean. Brain, vol. xxvi, p. 524.
Weiss. Arch. f. Augen., xxiii, 1891, S. 194.
Weiss. Über das Gesichtsfeld der Kurzsichtigen. Wiesbaden, 1898.
Wettendorfer. Deutschmann's Beiträge zur Aug., part 48.
Zentmayer and Posey. Comparative Value of Eserine and Iridectomy in Simple Glaucoma.

FURTHER CASES OF THROMBOSIS OF THE CENTRAL VEIN.

By George Coats, Curator.

In a former paper* on the subject of thrombosis of the central vein I showed that the pathological examination of affected eyes had so far led to confusion rather than to clearness. No fewer than six different lesions had been described by different authors as the essential basis of a very well-defined clinical entity. I reported four cases, in the hope of adding to the data available for retaining or rejecting this multiplicity of explanations, or, if possible, of bringing the several lesions into line under one dominating factor. At the same time the opinion was expressed that this could not yet be done with certainty, and that a greater number of fully-examined cases, with transverse serial sections through the region of the nerve entrance and lamina cribrosa, were required. Shortly afterwards I was able to report another case,† and since then I have collected 11 others, upon which the present paper is based.

An important contribution to the subject has been made by Harms‡ in a long and excellent paper. This author has reported two cases of arterial and 10 of venous obstruction. Of the latter, one seemed to be due entirely to obliteration of the vein from endo- and mesophlebitis, without thrombosis. One was due to an organised thrombus, apparently associated with a normal vein wall. Three were due to thrombosis associated with disease of the vein wall, the coagulum being laid down at the site of greatest disease in one, somewhat farther up the nerve in the other two. In one of these two the thrombus was canalised, the case resembling Case 2 of my former paper, which was the first recorded example

* R. L. O. H. Rep., vol. xvi, pt. i, p. 62, 1904.

† Trans. Ophth. Soc., vol. xxiv, p. 161, 1904.

‡ Arch. f. Ophth., vol. lxi, pt. i, p. 1.

of this condition. In two there was a thrombus in the vein, associated with advanced endarteritis in the artery; in one of these there was also a thrombus in the artery. In three cases no obstruction was found in the central vein, but in two of these the nerve entrance was cut longitudinally, and in one the nerve was divided very close to the globe, and there was a deep glaucomatous cup, so that almost no part of the central vein was available for examination; in two some of the retinal veins were thrombosed. From the consideration of his own cases, and of those recorded in literature, Harms comes to the conclusion that the following lesions have actually been proved by pathological examination in cases clinically diagnosed as "thrombosis of the central vein"; (1) Thrombosis of the vein. (2) Disease of the vein wall (endo- and mesophlebitis). (3) A combination of these two. (4) Very exceptionally (Yamaguchi) compression of the vein from without. He is also inclined to admit thrombosis of the retinal veins without obstruction of the central vein. He regards with the gravest suspicion (and in this I fully agree with him) recent attempts to explain such cases by lesions on the arterial side of the circulation. Where the whole course of the vein, and especially that part of it which traverses the lamina cribrosa, has not been examined in transverse sections, there is a strong probability that the essential lesion has been overlooked. The endarteritis may indeed be the cause of the ophthalmoscopic appearances, but not directly, only by slowing the blood current, and so favouring the deposition of a thrombus in the vein; this again will react prejudicially on the arteries. If such a thrombus is *not* formed in the vein, and if the endarteritis progresses sufficiently, the picture of obstruction of the artery is produced, not that of occlusion of the vein. This also has been definitely proved by pathological examination, Galinowsky,* Harms,† Coats,‡ etc.

* Arch. f. Augenh., vol. xliii, p. 183, 1901.
† *Loc. cit.*, Case 1.
‡ R. L. O. H. Rep., vol. xvi, pt. iii, p. 262.

Another example of a canalised thrombus has been reported by Sidler Huguenin.* The endothelium of the artery was extensively detached, and lay coiled up in the centre of the lumen, an appearance which the author believed to be due to stripping up by the blood current, such as occurs in dissecting aneurism. The thrombosis of the vein was supposed to be due to slowing of the blood current from this cause. It is by no means certain, however, that the condition in the artery was not in part an artefact. A somewhat similar condition of affairs will be described in some of the cases mentioned below.

Baquis† has also reported a case in which an organised thrombus was found in the vein in the region of the lamina cribrosa. In all these cases glaucoma followed the thrombosis at a longer or shorter interval.

Bartels‡ has studied the condition of all the ocular vessels in glaucoma, but without throwing any new light on the connection of that condition with thrombosis of the central vein.

Cases.

In the following cases the method of examination was the same as that described in my former paper. The eyes were all preserved in formalin, except where otherwise stated. The globe was cut in serial section, every fifth to tenth being mounted (in different cases), and others in the intervals where necessary. The nerve and nerve entrance were excised, and cut in transverse serial sections throughout their length. In addition to the ordinary staining methods, Weigert's elastic tissue stain was used, and rendered much assistance. I omit all unimportant details in the descriptions.

Case 1.—*Thrombosis of right central vein of doubtful, but probably short duration. No albuminuria or evidence of*

* Arch. f. Augenh., vol. li, p. 27, 1904.
† Festschrift f. Hirschberg, p. 33, 1905.
‡ Zeitsch. f. Augenh., vol. xiv, p. 103, 1905.

arteriosclerosis. Glaucoma. Excision about three weeks after its occurrence. Left eye normal throughout. In the bisected eye very numerous retinal hæmorrhages with large tortuous veins. Loosely reticular cellular mass in central vein in anterior layers of the lamina cribrosa. Obstruction terminated posteriorly by the accession of a collateral branch. Endarteritis in the central artery. Moderate changes in the retinal vessels. Corneo-iridic angle more occluded on the temporal than on the nasal side.

I am indebted to Mr. Lawford for the material and clinical notes of this case:—

A gentleman, aged 60, first consulted Mr. Lawford in January, 1903, when vision in each eye was 6/5, with a low hypermetropic correction. In September, 1904, he discovered that the sight of the right eye was defective. The vision at that time was 6/36; the papilla was thought to be somewhat cupped, but its colour was good; the tension was doubtfully raised; the field of vision was full. In December, 1904, a few spots of hæmorrhage were detected in the fundus, together with a small patch of whitish exudation. The veins bent abruptly at the edge of the cup; the retinal arteries showed a bright reflex. His doctor wrote that he had never found evidence of arteriosclerosis or high arterial tension; the urine had always been normal. Up to this date therefore there had certainly been no thrombosis of the central vein. The patient was not seen again until July, 1905, when glaucoma was present, and vision was totally lost. *The anterior chamber was deep*, T + 2. The eye had probably not been blind for more than a week. It was excised a fortnight later. Three months afterwards the patient was in good health. The left eye remained normal throughout.

Pathological Examination.

The globe is divided horizontally. The corneal surface is rough, the anterior chamber deep, the pupil slightly irregular owing to the presence of posterior synechiæ downwards and inwards. The lens is *in situ*, the vitreous free from hæmorrhage. The retina is strewn with very numerous hæmorrhages, chiefly

towards the posterior pole. The veins are very large and tortuous. The disc is cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is deeply excavated. On the side of the cup the veins are engorged, but have normal walls. Some of the arteries have also normal walls, while others are much narrowed by endarteritis. The central artery and vein are formed at about the same level in the anterior layers of the lamina cribrosa. The vein is no sooner formed than it becomes obstructed by a cellular mass (Plate IV, Fig. 1). This consists of a delicate reticulum, among which rather large cells are present with a distinct protoplasmic body and a pale nucleus. There are a few polymorpho-nuclear leucocytes, but no red corpuscles can be recognised with certainty. The vein wall is very easily seen, and is not collapsed or shrunken. The mass in the lumen has shrunk away from the wall in places, and in these situations some endothelial lining cells may be seen. They are absent, however, where the thrombus adheres to the wall. The vein wall itself, and the surrounding connective tissues, are absolutely free from inflammatory infiltration. This condition of affairs lasts throughout the whole thickness of the lamina cribrosa. Immediately beyond, it is terminated suddenly by a large collateral branch which enters at one side from the surrounding connective tissue, and restores the lumen (Plate IV, Fig. 2).

Owing to the considerable size of this twig, the vein almost immediately becomes normal again. It is filled with well-formed blood corpuscles. Farther up the nerve a slight degree of round-cell infiltration appears in the vein wall for a space, but otherwise it remains normal till the end of the series. The artery shows much endarteritis throughout its course. The whole intima, including the elastic membrane, has become detached, and lies as a collapsed mass in the centre of the lumen. This is probably an artefact. The nerve is highly atrophic. In places, the trabeculæ have become thickened, and have fallen together, giving an appearance of condensation to the nerve; in places they have retained their normal architecture, while the nerve fibres have entirely disappeared, leaving large lacunar spaces crossed by a network of supporting elements.

In the retina hæmorrhages are widespread, but usually small and confined to the internal layers. There are, however, some small subretinal hæmorrhages in the neighbourhood of the fovea. The nerve fibre, ganglion cell, and inner reticular layers are all much atrophied and œdematous; the inner nuclear to a less extent, while the outer layers are, on the whole, well preserved. At the fovea there is much distortion of the retinal elements, with loss of the pigment epithelium and adhesion to the atrophied choroid. The retinal vessels show only a moderate degree of thickening. The veins are much engorged.

The cornea is normal. The corneo-iridic angle is only very slightly occluded on the nasal side, but as far as the termination of the membrane of Descemet on the temporal. The measurements taken from the anterior end of the ciliary muscle as a convenient point are, nasally 0·22 mm., temporally, 0·76 mm. The iris stroma is condensed, cellular, and deeply pigmented. The lens measures 8·5 mm. in diameter. The ciliary body and choroid are highly atrophic. The ciliary vessels are normal.

The clinical history in this case does not give the exact date of the occurrence of thrombosis. When the patient was seen, in December, there were signs of vascular disease and a few small hæmorrhages. When seen again, in July, glaucoma had already supervened, and examination of the fundus was impossible. The macroscopical examination, however, showed the typical hæmorrhagic retinitis. From the microscopical examination it is evident that the thrombosis was of recent formation. The red corpuscles had disappeared, and the thrombus had been invaded by the endothelium. But there was as yet no proper organisation. No reaction had taken place in the surrounding connective tissues, the vein still retained its normal size and form and had not undergone the shrinkage and effacement which are found in old cases. The restoration of the lumen by the entrance of a collateral branch is exceedingly well illustrated. The marked degree of endarteritis was also a notable point.

CASE 2.—*Thrombosis of the right central vein in a patient, aged 74, suffering from arteriosclerosis and albuminuria. Glaucoma present two months later. Excision about two and a half months from onset of symptoms. Occlusion of the vein lumen by an organised cellular mass within the lamina cribrosa. Restoration of the circulation by the entrance of a large collateral branch from the trabeculæ of the nerve. Artery normal, and not much disease of the retinal vessels. Corneo iridic angle blocked only on the temporal side.*

This case was also under Mr. Lawford's care, and I am indebted to him for the clinical notes.

A gentleman, aged 74, noticed a sudden failure of the sight in the left eye in November, 1904. The urine contained albumen and the peripheral arteries were very rigid. He was seen by Mr. Beaumont, of Bath, who noted "R. retinal apoplexy with white plaques scattered about the fundus." On January 27, 1905, he was again seen, with "cyclitis and secondary glaucoma." On February 4 he consulted Mr. Lawford, who found moderate ciliary congestion, the iris discoloured and apparently swollen, the pupil small and irregular. There was no fundus reflex and the tension was + 2 fully. The eye was not very tender. It was excised on February 7, 1905. The left eye remained normal throughout. In March, 1906, his doctor reported that he was rapidly sinking from Bright's disease with anasarca and cardiac failure; there was no mention of an affection of the other eye.

Pathological Examination.

The globe is divided horizontally. *The anterior chamber is of average depth.* The corneo-iridic angle is blocked on the temporal, apparently normal on the nasal side. The lens is *in situ*. There is no vitreous or subretinal hæmorrhage. The retina is covered with numerous hæmorrhages of all shapes and sizes.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is not very deeply excavated, and the vessels on the side of the cup have normal

walls and contain blood. Immediately in front of the lamina cribrosa a normal artery and vein are formed in the usual manner. The lumen of the vein only remains free for a short distance. While still in the anterior layers of the lamina cribrosa it becomes encroached upon from one side by cellular fibrous tissue (Plate IV, Fig. 3). Organisation is well advanced in it, the stroma is distinctly fibrous, and the nuclei tend to have the elongated form of connective tissue cells. The tissue is not sharply marked off from its surroundings, and the proper wall of the vein cannot be traced with any certainty, so that it is doubtful whether it represents an encroachment from outside the wall or a cellular mass (probably proliferated endothelium) within the lumen. The appearances in subsequent sections, however, make the former more probable. At one side there is a small quantity of shrunken coagulum with a few polymorphonuclear leucocytes among it. The surrounding connective tissues are quite free from inflammatory infiltration. The obstruction is present over the whole length of the central vein within the lamina cribrosa, but is only complete over a very small area (three sections). Towards the posterior part of the lamina the vein wall is again traceable, and its lumen is filled with homogeneous coagulum in which many leucocytes, and here and there a few red corpuscles are present. A large collateral now emerges from the trabeculæ of the nerve, and plunges into this coagulum (Plate IV, Fig. 4). It carries with it a stream of normal red corpuscles, and hollows out a channel in the clot. From this point onwards the lumen of the vein is unobstructed and filled with red corpuscles. It is at first small, but soon becomes of normal size by the addition of other collateral twigs, and remains so to the end of the series. The artery is normal throughout. The nerve is considerably atrophied.

The retina shows hæmorrhages chiefly confined to the inner layers, but in places reaching as far as the outer nuclear. Most of them are small, but a few are large and have caused distortion of the retina. There are no vitreous or subretinal hæmorrhages. In general, however, the retina is well preserved except for considerable atrophy of the nerve fibre and ganglion cell layers. There is very little œdema and no coagula are found. The retinal vessels are not much diseased.

The corneo-iridic angle is practically free on the nasal side: a little blood is present in the anterior chamber and in the stroma of the iris root. On the temporal side, on the other hand, the angle is blocked nearly as far as the termination of the membrane of Descemet (0·51 mm.), and the root of the iris is somewhat atrophic. Otherwise the stroma of the iris is perfectly normal and free from infiltration. The cornea, ciliary body and choroid are normal.

The case resembles the last in its general features, but organisation is more advanced. The thrombus is limited, and the circulation is restored in the same way by the accession of a large collateral. It differs chiefly in the absence of endarteritis in the artery. The comparative slightness of the changes in the retina and in the retinal vessels is worthy of note; it is probably to be associated with the unusual freedom of the collateral circulation, and the short duration of the disease.

Case 3.—*Thrombosis of the left central vein of* 10 *days' duration in a man, aged* 47, *the subject of gout. During the next four months increase in the retinal hæmorrhages, and finally the occurrence of a large detachment of the retina below. Urine? Glaucoma a week or two later. Enucleation six months from onset of symptoms. Central vein occupied by a fully-organised mass a short distance behind the lamina cribrosa. Lumen not fully restored in the piece of nerve excised. Widespread thrombosis with organisation of the retinal vessels. Central and retinal arteries practically normal. Corneo-iridic angle blocked on the temporal side alone.*

I am indebted to Mr. Arnold Lawson for the material and for the clinical notes.

A gentleman, aged 47, had noticed a haziness before the left eye for 10 days. V.R., 6/9; V.L., 6/36. R. fundus normal; L. thrombosis of the central vein. He had had no recent illnesses, was not anæmic, and had never suffered from syphilis. He was said to be gouty, but had never had acute gout; a few days after he was seen, however, he had a definite subacute

attack, from which convalescence was very slow. Meanwhile the eye condition showed continuous retrogression, innumerable hæmorrhages appearing in every part of the fundus. Four months after the onset of symptoms the vitreous was still clear, but a large detachment of the retina had occurred below, probably from subretinal hæmorrhage. A week or two later the eye, which up to this time had retained perception of light, was suddenly attacked by acute glaucoma. This proved intractable, and the eye was excised six months after the first onset of symptoms, having been in a state of absolute glaucoma for about a month prior to operation. The right eye remained normal throughout. The patient has not since been heard from.

Pathological Examination.

The globe is divided horizontally. *The anterior chamber is deep.* The corneo-iridic angle is not obviously occluded. The lens is *in situ.* There is a moderate amount of hæmorrhage in the vitreous. The retina is suffused in every part with large hæmorrhages, and in front of the position of the papilla there is a yellowish mass through which the retinal vessels emerge. There is a large detachment of the retina downwards and outwards. The subretinal space contains coagulum tinged with blood.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is not very deeply excavated. On the side of the cup the arteries are somewhat sclerosed, the veins are normal but small. A single central vein is formed in the anterior layers of the lamina cribrosa, and remains normal throughout its thickness. At the posterior level of the lamina it suddenly becomes occluded and replaced by a little shrunken knot of fibrous tissue (Plate IV, Fig. 5). The matrix is indefinitely fibrous, and contains many oval nuclei. The mass has shrunk away from the surrounding tissues, but the space left is not part of the original vein lumen, since it contains no blood and is not lined by endothelium. As only a very short piece of nerve was excised with the globe, the series of sections ends before restoration of the lumen has occurred. The central artery is normal throughout. The nerve is not atrophic.

The retinal vessels are much diseased, especially the veins. The change in them is usually one of thickening of their connective tissue walls, without endothelial proliferation. Many of them contain organised thrombi very similar to that found in the central vein (Plate IV, Fig. 6). They are often surrounded by pigment granules and masses which seem to have collected in the perivascular lymph spaces. These are presumably derived from the blood pigment. The retinal arteries show both endothelial proliferation and thickening of their outer coats. The retina is infiltrated and destroyed by enormous hæmorrhages, which have also broken through both into the vitreous and into the subretinal space.

The cornea is normal. The corneo-iridic angle is blocked as far as the termination of the membrane of Descemet on the temporal side (0·5 mm.); there is not much condensation or atrophy of the adherent iris root. There is a moderate round cell infiltration around the canal of Schlemm. On the nasal side the angle is quite open. A few leucocytes and pigment granules are present among the spaces of Fontana. The iris tissue generally is condensed, and there are a few small patches of round cell infiltration in its stroma and also in the anterior part of the ciliary body. The ciliary body is somewhat atrophic; the choroid is normal. The lens measures 7·5 mm. in diameter.

The thrombus in this case was somewhat more fully organised than in the last, and the vein was becoming much shrunken. The extensive thrombosis of the retinal veins was an important point. It did not affect all the veins, so that some blood was still present in the chief branches on the side of the cup. The thrombosis in the retinal veins was also not directly continuous with that in the central vein. Between the place where the vein was formed by the meeting of its main retinal branches and the site of the thrombus there was a piece of vein with a clear lumen and more or less normal walls. The thrombi in the retinal vessels were therefore not formed directly by spreading of the process from the thrombus in the central vein, but were formed independently, presumably as a result of the

interference with the circulation. In spite of the definite history of gout, there was no evidence of inflammatory infiltration of the vein wall apart from the site of the thrombus.

CASE 4.—*Thrombosis of the left central vein of* 10 *days duration. T. slightly +. Anterior chamber of normal depth. Trace of albumen in the urine on one occasion only. Definite onset of glaucoma two months later. No improvement in spite of eserin and iridectomy. Excision four months from onset of symptoms. Occlusion and almost complete effacement of the central vein in the anterior part of the lamina cribrosa by a cellular organised mass. Extensive endarteritis. Retinal vessels much diseased. Corneo-iridic angle occluded equally on the two sides.*

I am indebted to Mr. Fisher for the use of the following clinical notes :—

A man, aged 60, came to the Royal London Ophthalmic Hospital on November 15, 1905, complaining of a mist before the left eye of 10 days duration. V.R. 6/6 with + 1·25 D sph. V.L. fingers at 20 cm. The left pupil reacted only slightly to light. The anterior chamber was of normal depth. The ophthalmoscope showed "thrombotic retinitis" with silver wire arteries. The tension was slightly raised. The urine on this occasion showed a slight trace of albumen, but this could not be detected on several subsequent examinations, and the specific gravity was usually about 1020; there was no glycosuria. Ten days later the retinal hæmorrhages were still more extensive. On January 24, 1906, he presented himself with a definite attack of glaucoma. The tension was + 2 or + 3, the cornea hazy, the pupil semidilated and fixed. *The anterior chamber was deep and remained so.* In spite of the use of eserin, etc., the tension remained high and an iridectomy was therefore performed on February 27. It was followed by much hæmorrhage from the iris and conjunctiva and no lowering of the tension was obtained. The eye was therefore excised on March 10, 1906. The right eye remained normal throughout.

Pathological Examination.

The globe is divided horizontally. The iridectomy wound is bulging. The pillars of the coloboma are free. The anterior chamber is deep and contains blood. The corneo-iridic angles seem to be occluded. The lens is large and is in contact with the ciliary processes all round its equator. The vitreous is clear. The retina is *in situ* and is strewn with innumerable streaky hæmorrhages, especially round the papilla. In the macular region there are many white spots, but no recent hæmorrhages. The retinal vessels are barely visible. The disc is cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—In the retina, in the neighbourhood of the papilla, the vessels show very great changes, especially the arteries. There is both endarteritis and thickening of the outer coats, the latter being often the seat of true hyalin degeneration, with loss of nuclear staining. Some of the vessels are completely occluded by these processes; the veins are enlarged and full of blood. Their walls are often much thickened and sometimes show localised round-cell infiltrations. There is no endothelial proliferation.

The branches of the central vein unite into a common trunk immediately in front of the lamina cribrosa. This is no sooner formed than it becomes collapsed and blocked by a shrunken cellular mass. The ground substance is homogeneous; the cells are oval or elongated. There are no red corpuscles or polymorphonuclear leucocytes. Towards the posterior part of the lamina the shrinkage becomes less extreme, a few red corpuscles and leucocytes are visible in the homogeneous mass, and at the same time a distinct round-cell infiltration appears in the surrounding connective tissue (Plate V, fig. 7). The vein lumen then becomes free once more and has a normal endothelial lining, but it is still very small, while the walls are thick and somewhat infiltrated. The lumen speedily enlarges, while the infiltration becomes less. Some distance up the nerve there are two small areas of endothelial proliferation, but they do not materially narrow the lumen, and are only present for a very short distance. The lumen remains patent, and filled with blood as far as the end of the series.

The artery in its whole course behind the lamina is extensively diseased, especially posteriorly. The changes are entirely within the lamina elastica. Next to this membrane comes a layer four or five deep of large, pale, blown-out cells, usually with eccentric nuclei. The limits between cell and cell are fairly clear; the protoplasm is very faintly stained and slightly granular. Within this there is a layer of dense laminated tissue with nuclei elongated transversely. The lumen is narrow, filled with blood, and situated quite eccentrically. Its endothelium is well preserved. Elastic staining shows the presence of fine fibres among the dense tissue immediately beneath the endothelium, but not among the blown-out cells. It seems probable that these cells are not derived from the endothelium, which forms an unaltered layer lining the lumen, but from the subendothelial tissue normally present between the endothelium and the elastic lamina. The papilla is deeply cupped and the nerve is atrophied and shrunken.

Hæmorrhages in the retina are less abundant than usual. They are probably becoming absorbed, as large areas are found where the retinal tissues are destroyed, although there are only a few red corpuscles. As usual, the outer layers—rods and cones, and outer nuclear—are much the best preserved; the inner are almost totally destroyed towards the posterior pole, better preserved in the periphery. The retinal vessels show the same changes as have already been described on the papilla.

The corneal epithelium is œdematous, the stroma normal. The corneo-iridic angle is occluded on both sides to a point a little beyond the termination of the membrane of Descemet. The occlusion is equal on the two sides (about 0·77 mm.). There is evidence of considerable old iritis. A thin fibrous membrane stretches across the pupil. There is a layer of new-formed fibrous tissue on the front of the iris, which has caused ectropium uveæ by its contraction. Among this tissue and in the angle of the anterior chamber there are a few blood corpuscles. The iris stroma is much condensed and deeply pigmented. The ciliary body is atrophic. There is much sclerosis of the choroidal vessels, especially the arteries. The ciliary arteries also, both anterior and posterior, show endarteritis. The lens measures 8 mm. in diameter.

The case is an example of the commonest type of pathological lesion, a thrombus fully organised, and causing total obliteration and almost complete disappearance of the vein. The slight cellular infiltration of the walls of some of the retinal vessels may be associated with the inflammatory reaction in the anterior part of the eye due to the iridectomy. The case also furnishes a good example of the association of advanced endarteritis with thrombosis of the vein. Glaucomatous changes at the corneo-iridic angle and in the papilla were marked.

Case 5.—*Thrombosis of the left central vein in a woman aged* 60. *Much cardiac hypertrophy and general arteriosclerosis; no albuminuria. Eight to ten months later glaucoma. Enucleation* 12½ *months from onset of symptoms. Slight contraction of field of vision, and lens opacities in right; no retinal hæmorrhages. Total obliteration of the central vein in the region of the lamina cribrosa by a cellular organised thrombus. Gradual restoration of the lumen by the accession of small collateral twigs. Advanced endarteritis in the central artery. Retinal vessels much diseased. Corneo-iridic angle more occluded on the temporal than on the nasal side.*

I have to thank Mr. Lang for permission to use the clinical notes of this case.

A woman, aged 60, came to the Royal London Ophthalmic Hospital on May 19, 1904, complaining of dimness of vision of the left eye. A diagnosis of thrombosis of the left central vein was made. V.R. with −4 D sph. = 6/9; V.L. = 6/18 not improved. There were slight lens opacities in both eyes, but the right fundus was normal. There was marked general arteriosclerosis and cardiac hypertrophy, but no albuminuria. Ten months later she returned with glaucoma of the left eye, the cornea hazy, the pupil dilated and fixed, the tension + 2. The eye had been painful for two months. It remained glaucomatous in spite of treatment, and as vision was totally lost, it was enucleated on June 3, 1905. A slight contraction of the field of vision was noted in the right eye in May, 1905, otherwise it remained normal throughout.

Pathological Examination.

The globe is divided horizontally. The cornea is clear, *the anterior chamber of normal depth.* The iris pattern is not obscured, the corneo-iridic angles appear to be occluded. The vitreous is free from hæmorrhage. The retina is *in situ*, and shows a moderate number of hæmorrhages, especially in the temporal periphery. The disc is deeply cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—There is deep glaucomatous cupping. On the side of the excavation the vessels, both arteries and veins, are exceedingly small and thick walled. The arteries especially are narrowed almost to obliteration by endarteritis and thickening of the middle coat. The main artery is formed at the bottom of the cup, the vein somewhat farther back in the anterior layers of the lamina cribrosa. Almost immediately it becomes occluded. The obstruction consists of a finely fibrillar tissue with a number of rather large oval nuclei in it, together with a few red corpuscles and polymorphonuclear leucocytes (Plate V, Fig. 8). It is difficult to say whether the oval cells are derived from the endothelium or from the surrounding connective tissue cells. The former seems more probable, since the cellular knot is entirely within an area of the normal size of the vein lumen, and there is absolutely no cellular infiltration of the surrounding connective tissues. The lumen of the vein is completely filled; there is only a small cleft at one side, which is probably artificial, since it is not lined with endothelium. In the succeeding sections red blood corpuscles entirely disappear from the tissue, and it becomes much denser and less cellular, a few polymorphonuclear leucocytes still remaining, however. The nodule still completely fills the vein. The tissue now becomes much more cellular again, the nuclei being more like those of ordinary connective tissue. The ground substance is also more definitely fibrous. The shape and appearance of a vein is entirely lost, there is no trace of a lumen or vein wall, merely a little cellular knot without definite boundaries in the position which it ought to occupy (Plate V, Fig. 9). The connective tissue around the vessel remains free from all infiltra-

tion except in this position. This condition remains for a very considerable distance. Finally, however, a minute branch from the surrounding tissues plunges into the knot, and taking up a central position in it, restores a minute blood filled and endothelium lined lumen in the normal position of the vein (Plate V, Fig. 10). Very gradually other similar collaterals are added, but even up to the last sections of the series the lumen is by no means restored to its original size, while the wall of the vein remains very thick, and shows a considerable infiltration of round cells. The surrounding connective tissue remains quite free from round cell infiltration.

Throughout its whole course in the nerve the artery shows a very marked and somewhat peculiar endarteritis (Plate V, Figs. 8, 9, 10). It represents a more advanced condition of the condition shown in Fig. 11 of my former paper. There is a small and very eccentrically placed lumen. This is lined by a single layer of apparently normal endothelial cells. Between these and the elastic lamina there is a thick layer of cells, with large somewhat pale nuclei and swollen vacuolated bodies. Some of them are very large, contain many nuclei, and have all the appearance of small giant cells (Plate V, Fig. 10). Giant cells have been described in endarteritis by v. Michel.* Close to the endothelium the cells are less swollen, and their nuclei tend rather to be elongated. These cells show a great tendency to break down, so that between the endothelium and the elastica there is often simply a space filled with granular detritus. There are a few short elastic fibres among the cells, but they also have largely broken down. In places the elastica itself has become detached, but this is probably an artefact.

The nerve is very atrophic; practically no fibres remaining. In parts the trabeculæ have fallen together, so that the nerve is much condensed; in parts this has not occurred, and empty spaces are left, crossed only by the neuroglial supporting structures.

In the retina the veins show a very considerable thickening of their connective tissue walls, without endothelial proliferation. The lumen is concentrically narrowed. In places the nuclear staining is very imperfect, and there is probably true hyaline

* Zeitsch. f. Augenh., vol. ii, p. 1, 1899, Plate I, Fig. 2.

degeneration. The walls of the arteries are also thickened, but not so much so as in the case of the veins. There is no endothelial proliferation. The retina shows comparatively few hæmorrhages. Its inner layers—nerve fibre, ganglion cell, inner reticular and inner nuclear—are much atrophied, its outer well preserved. There are no subretinal or vitreous hæmorrhages The cornea is normal, the iris and ciliary body are much condensed and atrophic; there is slight ectropium uveæ. The corneo-iridic angle is occluded on both sides, but considerably more on the temporal (1·31 mm. as against 0·85 mm). There is some vascular disease of the choroid, but no imflammation. The lens measures 8·5 mm. in diameter.

The case shows in a typical manner all the lesions most commonly found in cases of thrombosis of the central vein. The mass occupying the vein lumen within the lamina was no doubt a portion of the original thrombus not yet fully organised. Then follows a considerable area in which organisation is very advanced, and has caused obliteration and almost complete disappearance of the vessel. Finally the lumen is gradually restored by the accession of small collaterals from the trabeculæ and surrounding connective tissue, but the wall remains thick and infiltrated for a space. The advanced state of organisation is to be associated with the long duration of the case.

Case 6.—*Thrombosis of the left central vein in a man aged* 31. *Onset probably during an attack of influenza a fortnight before. History of syphilis. Glaucoma already present when first seen, and fundus invisible. No improvement with eserin and paracentesis. Enucleation about four to six months from the onset of symtoms. Marked inflammatory infiltration of the central and all the retinal veins. Complete obliteration of the central vein for a short distance within the lamina cribrosa. Central artery normal throughout, except for slight infiltration of its walls. Root of the iris widely adherent to cornea. Extreme condensation of iris and octropium uveæ.*

I am indebted to Mr. Holmes Spicer for the use of the following notes:—

A man, aged 31, came to the Royal London Ophthalmic Hospital on November 10, 1905, complaining of dimness of vision in the left eye. He was uncertain as to its duration, but vision had been quite good in this eye 3 to 5 months before. It had failed especially within the last fortnight, after an attack of influenza. The eye had been painful for three days. Two and a-half years before, he had had a chancre. Six months later he had "rheumatism" of the knees, ankles, and elbows. The left eye at that time was red and watery, and the lids were swollen (?syphilitic iritis). V.R. 6/5. Eye normal in every respect. V.L. fingers at 6 in. Projection good. There was considerable lacrymation and photophobia, with ciliary and conjunctival congestion. The cornea was slightly hazy, and there were some fine precipitates on the back of it. *The anterior chamber was deep.* The pupil was regular and dilated to an extreme degree, only a narrow rim of iris about 1 mm. wide being visible. The iris was dull and new vessels were present on its surface. There were many large opacities in the vitreous, so that although a good red reflex was obtainable in all directions, no details of the fundus could be observed. The tension was + 1. A provisional diagnosis of cyclitis was made.

Treatment with eserin, etc., had no effect in reducing the tension or contracting the pupil, and a paracentesis was therefore performed on November 31. This also was without effect on the tension, and was followed by a large hyphæma. The eye remained painful, and was therefore excised on December 1. The right eye remained normal throughout.

Pathological Examination.

The globe is divided sagittally. The cornea is hazy, the anterior chamber deep. The iris is very short, adherent to the back of the cornea over most of its extent. There is marked ectropium uveæ. The lens measures 9·5 mm. in diameter. The vitreous contains a considerable amount of blood. The retina is strewn with numerous small punctiform hæmorrhages. The veins are large but not very tortuous. The disc is cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is moderately deeply excavated. On the side of the cup the veins are greatly engorged and show a very marked infiltration of their walls, with round cells. They are not thickened. The arteries are normal. At the level of the bottom of the cup, and while still in front of the lamina cribrosa, the vein suddenly becomes collapsed, and its lumen, previously distended with normal red blood corpuscles, contains a small quantity of shrunken homogeneous coagulum, which adheres to the wall at one side. The round-cell infiltration of the wall is considerable, and encroaches a little on the lumen. The surrounding connective tissues are also infiltrated. In the next sections the encroachment on the lumen becomes complete, so that it ceases to be traceable. For a short space the position of the vein is quite indistinguishable. Soon, however, it reappears again in the same position relative to the artery as before. A conical mass of organised tissue projects into its lumen, leaving only a little cleft at one side, which is filled with homogeneous coagulum similar to that found on the other side of the obstruction (Plate V, Fig. 11). The lumen quickly increases at the expense of the conical mass, and very soon reattains its normal size. All these changes are completed before the vein emerges from the posterior surface of the lamina. The cause of the restoration is not evident in this case; no considerable collateral vessel can be seen to enter the vein. Until the end of the series the vein remains of normal calibre. The wall is throughout moderately infiltrated with round cells, but is unthickened. The artery is normal in its whole course. The nerve is only slightly atrophied.

The retinal vessels show very advanced changes. All the large veins are surrounded by a thick layer of round-cell infiltration. This is not merely in the perivascular lymph sheaths but also in the vein wall itself (Plate V, Fig. 12). The lumen is considerably invaded. In places also there are organised thrombi within the veins, but these are generally of limited extent. These various processes not infrequently cause total obliteration of the vessels, in other places again they are much distended. The arteries also show some infiltration of their walls and proliferation of their endothelium, but to a very

much smaller extent than the veins. They are usually empty. There is a slight general infiltration of the inner layers of the retina, and some small patches of choroido-retinitis are present about the equator. The nerve fibre and ganglion cell layers, especially the latter, are somewhat atrophic; the outer layers are œdematous, but on the whole well preserved. In the retina itself hæmorrhages are comparatively small and scanty, but they are abundant in the vitreous. Many blood corpuscles lie on the anterior surface of the retina, and among them there are delicate fibres with elongated nuclei upon them. These often form thin membranes of considerable extent, fused with the retina in places, but in others separated from the limitans interna by a distinct space. They are sometimes supplied with small twigs from the retinal vessels. They undoubtedly represent commencing organisation of the blood in the vitreous—an early stage of retinitis proliferans.

The iris stroma is condensed and cellular. The root of the iris is adherent to the back of the cornea equally above and below; the adhesion extends beyond the termination of the membrane of Descemet, and the root of the iris is atrophic. There is marked ectropium uveæ, caused by the contraction of a new-formed fibrous layer on the front of the iris. The sphincter pupillæ has also a sharp forward kink near its inner end. There is blood in the anterior chamber. The fibrous tissue on the front of the iris closely resembles that on the anterior surface of the retina, and has probably been formed in the same way—by the organisation of blood extravasations. The cornea is normal, the ciliary body and choroid are atrophic, but free from infiltration. The lens has dropped out of the sections.

The case shows a quite unusual degree of inflammation, which is mostly confined to the walls of the vessels, especially the veins. It is evident that these are not the ordinary processes of angiosclerosis—that some toxic agent has probably been circulating in the vessels. According to the clinical history this was probably the toxine of influenza. I have already pointed out that a history of influenza is comparatively frequent in cases of thrombosis, especially in

those occurring in young subjects who do not show signs of arteriosclerosis. The occurrence of retinitis proliferans is also very possibly to be associated with a toxic condition of the blood, since, as Flemming has shown, that disease, although associated with hæmorrhage, probably also requires a circulating toxine for its production. Harms mentions the occurrence of influenza in two of his cases (Cases 3 and 9), and one of these was aged 20.

The changes in the iris most probably dated, in part at least, from the eye trouble which followed the syphilis two years before. They were much too advanced to coincide with the comparatively short history which he gave of his present attack. The extreme dilatation of the pupil, which was the most remarkable point in the clinical history, was due partly to the ectropium uveæ seen through a hazy cornea, partly to the shortening of the iris by the contraction of the new-formed fibrous tissue on its anterior surface.

Case 7.—*Thrombosis of the left central vein in a woman aged* 30, *probably of three months' duration. Onset of glaucoma shortly after first visit. No improvement with eserin and paracentesis. Excision about four months from commencement of symptoms. Obliteration of vein, with imperfect canalisation in the posterior layers of the lamina cribrosa. Round-cell infiltration of connective tissue around retinal and central veins. Corneo-iridic angle equally occluded on the two sides.*

I am indebted to Mr. Lang for the use of the case.

A woman, aged 30, came to the Royal London Ophthalmic Hospital on December 8, 1904, complaining of failure of vision in the left eye, of three months' duration. V.R. 6/6. V.L. perception of light. The opthalmoscope showed typical thrombosis of the central vein in the left. There was no evidence of syphilis. She had suffered from bilious attacks, with vomiting and headache, within the previous two to three years. The urine contained a trace of albumin and a few granular casts. She returned in three weeks, complaining of pain in the left eye. It was glaucomatous, the pupil semidilated and fixed, the anterior

chamber rather shallow. There was moderate circumcorneal congestion, a small hyphæma, and the tension was +1. Perception of light was completely lost. The disc of the right eye had somewhat blurred edges, but vision was still 6/6, the field full, and the tension normal. Eserin was used and a paracentesis performed, but without any good result, and as the eye remained painful, it was excised on January 8, 1905. In March, 1905, according to a communication from her husband, she was in good health and her other eye was unaffected.

Pathological Examination.

The globe is divided horizontally. *The anterior chamber is of average depth.* The lens is *in situ.* The vitreous contains exudation and a little hæmorrhage. A whitish-yellow mass lies over the position of the disc. There are very numerous hæmorrhages, especially in the neighbourhood of the disc, on the nasal side; somewhat fewer temporally. A large subretinal hæmorrhage is present below.

Microscopical Examination—

Optic Nerve and Central Vessels.—The disc is only moderately excavated. Within the cup, and in the vitreous in front of it, there is a quantity of hæmorrhage and coagulum. This is becoming invaded by fine vascular connective tissue, which springs from the lining tissue of the cup. The veins on the side of the cup are much thickened, the lumen being narrowed in a concentric manner. There is slight round-cell infiltration around their walls, but the thickening itself, which affects the fibrous tissue of the wall, is not unduly cellular. The endothelium is not proliferated. The arteries are normal.

At the bottom of the cup a single artery is first formed, and a few sections farther back the vein appears. There is a very distinct round-cell infiltration of the connective tissues around the vessels. Both contain blood. Some small hæmorrhages are present in the substance of the nerve at this level. Towards the posterior surface of the lamina the vein very suddenly becomes obliterated. Its situation is marked by an area of round-cell infiltration, among which a few blood corpuscles are present. There is however no lumen, and its wall cannot be traced. The cellular infiltration has no definite outer boundary, but is

lost gradually in the surrounding connective tissues. The artery at the same point shows for the first time some vacuolation and proliferation of its endothelium. A few sections farther back three small lumina appear within the little cellular knot (Plate VI, Fig. 13). Each is lined with endothelium and contains homogeneous coagulum, with here and there a few red blood corpuscles. So far as can be determined, they do not arise by the entrance of vessels from without, but represent channels formed *in situ* from the proper venous lumen beyond. They represent therefore an incomplete stage in a process of canalisation. Following the vein up the nerve, a single lumen is speedily reformed. It remains small, and the wall of the vein is infiltrated for some distance, but with the entrance of several accessory branches the lumen slowly enlarges, while at the same time the infiltration gradually subsides, so that before the end of the series the wall is again normal. Over the area of greatest change in the vein the artery shows a moderate degree of endarteritis, but this also disappears again farther up the nerve. The nerve itself is much atrophied.

The retinal vessels show changes similar to those already described on the side of the cup. Hæmorrhages are extremely abundant in and beneath the retina, and also in the vitreous. The retina is much distorted by them, and there are large coagula in the internuclear layer. Over the whole of the posterior part of the retina there is a comparatively thick layer of connective tissue. It is dense and cellular on its inner side, somewhat looser externally, and its vessels are numerous but small. Over a large part of its extent it has no connection with the retina, and it is intimately connected with it only at the papilla. In the periphery it ends in fine threads, which sometimes become attached to the surface of the retina and sometimes disappear among the vitreous hæmorrhages. Probably by its contraction the retina has been thrown into a number of folds, and the limitans interna shows many much finer crenations. The case furnishes, in short, a good example of retinitis proliferans.

With regard to changes in the anterior part of the eye, the cornea is normal. The stroma of the iris is atrophic and condensed. There is a thin layer of new-formed fibrous tissue on its

anterior surface, which has caused ectropium uveæ with anterior kinking of the sphincter. The angle of the anterior chamber is shut off by adhesion of the root of the iris about equally on the two sides (0·85 mm.). The ciliary body is atrophic and the choroid is normal. The lens measures 8·25 mm. in diameter. There are no signs anywhere of recent inflammation.

The resemblance between this case and Case 6 reported above should be noted. In both the patient was unusually young (31, 30), the ordinary changes of angiosclerosis were conspicuously absent, while, on the other hand, there was considerable inflammation of the vein walls. At the site of obstruction also the signs of inflammation were unusually prominent. In both there was retinitis proliferans, and in both there was probably a toxic condition of the blood (influenza, and perhaps syphilis in Case 6, albuminuria in Case 7). In both there was new-formed fibrous tissue on the front of iris, with ectropium uveæ. They show therefore a coincidence on a number of more or less unusual points, which seems to indicate that they should be classed together, and somewhat apart from the others. I shall discuss this later.

In the present instance also the obstructed area was unusually small; it occupied only some six sections. The case furnishes a good example of an early and incomplete stage of canalisation, which is an unusual condition in thrombosis of the central vein. I have described and figured a more advanced stage of the same condition in Case 2 of my former paper, and a similar condition has since been reported by Sidler-Huguenin, and by Harms.

Case 8.—*Failure of sight in a man, aged* 61, *the subject of arteriosclerosis. Onset of glaucoma six weeks later. Iridectomy followed by expulsive hæmorrhage. Enucleation. Organised thrombus in the vein in the posterior layers of the lamina cribrosa.*

I am indebted to Mr. Percy Flemming for the material and notes.

A man, aged 61, came to University College Hospital with symptoms of glaucoma in his left eye. He gave a history of failure of sight in that eye for six weeks before it became painful. The tension was +2 and all the signs of glaucoma were present. Vision was reduced to perception of light in the temporal field only. The peripheral arteries were rigid and there was cardiac hypertrophy. The urine contained no albumen or sugar. The fundus was invisible, but, in view of the history, hæmorrhagic retinitis was suspected. As the glaucoma did not prove amenable to treatment, an iridectomy was performed. This was followed by expulsive hæmorrhage, and the eye was enucleated.

Pathological Examination.

The globe is divided sagittally. The corneal wound is laid back in the form of a flap, and the intraocular contents are prolapsed into it. The eye is full of blood clot, and the intraocular structures are barely distinguishable.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla shows a moderately deep glaucomatous cup, which is filled with hæmorrhage. The veins on its side are much engorged, and their walls are considerably infiltrated with polymorpho-nuclear leucocytes. This infiltration, however, does not extend beyond the lamina, and is probably a sign of commencing infection of the eye due to tearing open of the wound by the intraocular hæmorrhage. The arteries are infiltrated as well as the veins; they are well filled with blood and show no endarteritis. Towards the posterior part of the lamina cribrosa the vein suddenly becomes very small, and its lumen contains some shrunken homogeneous coagulum pressed up against one wall, as well as some red corpuscles. Presently the whole lumen becomes filled with the clot, all formed red corpuscles having disappeared. The coagulum at the same time becomes more fibrillar, with little spaces and clefts among the fibrils. It becomes invaded by spindle-shaped cells with elongated nuclei (Plate VI, Fig. 14). There is no round-cell infiltration of the surrounding connective tissues, and the outline of the vein is not entirely lost. This condition lasts for a considerable distance above the lamina cribrosa; then a small

vessel finds its way into the cellular knot, and a little empty lumen is restored. It speedily enlarges by the entrance of collaterals, but does not regain its normal size for some distance. The wall is not at all thickened and the vessel remains empty and collapsed, but without inflammatory infiltration of its wall.

Over the whole area in which the vein is obstructed the artery is normal and distended with blood. Higher up the nerve, however, its lumen becomes very considerably narrowed by endarteritis, which gradually increases in ascending the nerve, so that in the last sections only a very small and eccentric lumen remains. The nerve is very highly atrophic, in places much condensed, in places loose in structure and œdematous.

The intraocular hæmorrhage is chiefly sub-retinal, partly also sub-choroidal and in the vitreous. The lens and most of the vitreous have been expelled. The retina, iris and ciliary processes are prolapsed into the wound. There are many hæmorrhages in the substance of the retina; the retinal vessels show infiltration of their walls with polymorphonuclear leucocytes, but no angiosclerotic changes. The iris stroma contains abundant hæmorrhage. The ciliary vessels are normal, and the choroidal do not show much sclerosis.

The association of thrombosis of the central vein with expulsive hæmorrhage does not seem to have been observed before. Possibly this is because the central vein is not usually examined in these cases. I do not believe, however, that thrombosis of the vein is a common cause of expulsive hæmorrhage. In the first place, so far as the records at my disposal go, it would seem that when iridectomy is performed upon such eyes, and when the eye is subsequently lost, the loss is not usually due to expulsive hæmorrhage, but to return of the glaucoma with gaping of the wound, etc. Again, in almost all cases of expulsive hæmorrhage the effusion is sub-choroidal, not retinal, sub-retinal or intravitreous, as might be expected if it were due to a block on the central vein. Naturally, however, if there were an obstruction of the vein, one would expect the retinal vessels to add their quota to the hæmorrhage, as they evidently did in the present instance.

CASE 9.—*Gradual loss of vision in the left eye during* 16 *months, then sudden and complete failure. Ophthalmoscopically, thrombosis of the central vein. T. n. in both. One month later left glaucoma. Enucleation about* 18½ *months from onset of symptoms. Great narrowing of the vein behind the lamina, apparently from endothelial proliferation. Capillary channel still present. Retinal arteries and veins much diseased. Corneo-iridic angle more occluded on the temporal than on the nasal side.*

I am indebted to Mr. Lang for the use of this case.

A man, aged 58, came to the Royal London Ophthalmic Hospital on December 4, 1905, complaining of gradual failure of the vision of the left eye of 16 months' duration. Vision had then failed suddenly and completely. When seen five days later the typical picture of thrombosis of the central vein was present. The tension was normal in both eyes. V.R. 6/6; fundus normal. V.L. Perception of light. The urine contained no albumen or sugar. About 2½ months later he reappeared with symptoms of glaucoma in the left eye, dusky pericorneal congestion, hazy cornea, slightly shallow anterior chamber, pupil moderately dilated, T + 1. The eye remained painful in spite of treatment, and was therefore excised a week later.

Pathological Examination.

The eye is divided horizontally. The cornea is hazy, *the anterior chamber fairly deep*. The iris markings are very clear. The corneo-iridic angle seems to be occluded for a short distance. The lens is large, and almost fills the interciliary space. The vitreous contains a few flocculi of exudation, no hæmorrhages. The retina is *in situ*, and is infiltrated in every part with large hæmorrhages. The vessels are invisible. The disc is not cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—In front of the lamina cribrosa there is a considerable endarteritis in the main branches of the artery. The veins are also thick walled. They are distended with blood. In the anterior part of the lamina a round-cell

infiltration appears at one side of the vein. The vessel contains homogeneous coagulum, with only here and there a red blood corpuscle. At the same time the endothelium thickens greatly, forming a layer several cells thick. The intima has partially shrunk away from the connective tissue wall, probably artificially. The round-cell infiltration soon ceases, but the thickening of the intima progresses gradually, so that a short distance behind the posterior level of the lamina the lumen is reduced almost to capillary dimensions (Plate VI, Fig. 15). It measures 8μ instead of 120μ to 140μ. The obstruction does not seem to have been absolutely complete, however; a minute stream was probably present during life. The tissue obstructing the vein is not of the usual type, it has a definite concentric lamination, and contains elongated nuclei, which also have a concentric arrangement. It encroaches on the lumen from all sides, but leaves a central free portion containing blood. Altogether the appearance is more suggestive of proliferation of the endothelium (endophlebitis) than of organisation of a thrombus. Weigert's elastic tissue stain shows no elastic fibres among the proliferated cells. The disease of the vein wall ceases rather suddenly; the thickening of the intima is no longer present all round, but becomes confined to a bud-like excrescence on one wall. This shortly disappears, leaving a somewhat small, but otherwise normal vein. The vessel soon enlarges, by the accession of large trabecular branches, and remains of full size till the end of the series. The artery is normal throughout. The nerve is only slightly atrophic, solitary loculi being often singled out.

The retinal veins are much diseased, especially those of large and medium size. The lesion seems to be a combination of thickening of the connective tissue wall and endothelial proliferation. There is no evidence of thrombosis in any of the retinal vessels. The arteries are also thick walled, but are much less diseased than the veins; there is no endothelial proliferation. The retinal hæmorrhages are in general small but diffuse, so that while no considerable part of the retina is free, the retinal layers are usually well preserved. In the neighbourhood of the macula, however, there are some very large hæmorrhages, with large blood-filled spaces between the nuclear layers, and destruction of the retinal tissue.

The disc is not cupped, and the nerve is atrophic only in patches, which probably corresponded to portions of the retina destroyed by hæmorrhage.

The cornea is normal. The angle of the anterior chamber is occluded for a short distance on both sides, but decidedly more on the temporal; the measurements are, nasal 0·342 mm., temporal 0·461 mm. The iris stroma, ciliary body and choroid are perfectly normal and free from infiltration. The transverse diameter of the lens measures 8 mm.

This case seems to furnish an example of obstruction of the central vein brought about not by the formation of a thrombus within it, but entirely by narrowing of the lumen owing to disease of the wall. There was evidence that a minute and quite insufficient blood stream had been present throughout the whole course of the disease. A gradually increasing disease of the vein wall would accord well with the somewhat unusual history of a gradual loss of vision during sixteen months. The sudden loss of sight two months before he was seen probably corresponds to the occurrence of the specially large hæmorrhages found in the macular region.

The case shows well the early stage of glaucoma following thrombosis. Glaucoma had probably lasted some 12 to 14 days when the eye was excised. Inflammatory infiltration was entirely absent from the iris stroma or root. The iris was adherent, but only loosely and for a short distance. There was no atrophy or condensation of the tissue. As is extremely common in these early cases, the adhesion was more extensive on the temporal side.

Case 10.—*Ophthalmoscopic appearances resembling those of thrombosis of the left central vein, except that both the veins and arteries were extremely small. Duration doubtful. Three months later, glaucoma. Excision about a month from onset of glaucoma. Organised thrombus in vein within lamina cribrosa. Complete obliteration of artery in anterior layers of lamina by a nodule of endarteritis. Extensive thrombosis of*

retinal veins. Occlusion of corneo-iridic angle greater on the temporal side.

I am indebted to Mr. H. Parker for the material and clinical notes of this case, and to Mr. W. I. Hancock for obtaining them for me.

A woman, aged 34, came to the Central London Ophthalmic Hospital on December 29, 1904, complaining of loss of vision of the left eye. The opthalmoscope showed numerous large hæmorrhages all over the fundus. The disc was white, and both arteries and veins were barely visible. The pupil was inactive to light and the tension was normal. The right eye was normal; V. with −0·75 sph. 6/6. She had suffered from joint pains at intervals since she was 15 years of age, but there was no history of rheumatic fever. The heart, lungs, and urine were normal. On March 30, 1905, she reappeared, with glaucoma of the left eye of three days' duration. T. + 1½. There were no signs of iritis and no cupping of the disc. Eserine produced no improvement, and the eye was therefore enucleated about a month after the onset of glaucoma.

Pathological Examination.

The globe was preserved in Müller's fluid. It was divided horizontally. The depth of the anterior chamber is not noted. The aqueous and vitreous contain coagulated exudation but no blood. The angle of the anterior chamber appears to be occluded. The lens is *in situ*. The retina is *in situ*, and is strewn in every part with hæmorrhages.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is excavated. The cup is filled with a coagulated exudation, and there is also a quantity of delicate new-formed fibrous tissue (retinitis proliferans). It partially clothes the sides, and fills in the bottom of the cup. It consists of a delicate meshwork of fibres with elongated nuclei. At one spot, however, the tissue is denser, and is occupied by a large number of small convoluted blood vessels. These are supplied by vessels which arise from small twigs, probable veins, in the substance of the papilla.

The vessels on the side of the cup are small, and for the most part empty. Their walls show much thickening of the "fibrosis" type, with concentric narrowing of the lumen. The endothelium is not proliferated. The description applies to both arteries and veins.

Towards the bottom of the cup the lumen of the artery becomes very small and collapsed, and in the superficial layers of the lamina it is completely obliterated by endarteritis (Plate VI, Fig. 16). The muscular coat is intact; among the proliferated cells small curly elastic fibres are visible. The obstruction lasts for only a short distance; while the vessel is still within the lamina the endarteritis gives place to homogeneous coagulum, and before long red blood corpuscles are again found. The artery soon becomes free from endarteritis, and remains so till the end of the series.

The vein commences to be obstructed as soon as it is formed. At first its lumen is very wide, and contains granular *débris*, among which pale elongated nuclei of endothelial cells and a few delicate fibrils are visible (Plate VI, Fig. 16). Gradually the cells become more numerous and the fibrils more distinct, forming a close meshwork. The connective tissue wall of the vein also seems to take part, the cells contributed by it being smaller, rounder, and more deeply stained than those contributed by the endothelium. In places a group of cells of the endothelial type is found in the centre, surrounded by a ring of cells of the connective tissue type. Finally the tissue becomes denser and less cellular (Plate VII, Fig. 17). The obstruction occupies a very considerable length of the vein, much greater than in the case of the artery. It ends rather abruptly in a bluntly conical process at the point of entrance of a minute collateral branch. This occurs only in the last few sections of the series, so that the state of the vein wall beyond the seat of obstruction cannot be described with certainty. The nerve is very atrophic and condensed.

The retinal veins show extremely advanced changes, evidently due to the organisation of thrombi within them. In places they are represented merely by little shrunken knots of cellular tissue; in places one, or sometimes several, small lumina are present, probably the result of canalisation. In many places there are

collections of brown pigment granules around the veins. The arteries are collapsed and thick walled, but do not show much endothelial proliferation.

The retinal hæmorrhages have for the most part been absorbed, but the retina is extremely degenerated. The nerve fibre, ganglion cell, and inner reticular layers have disappeared altogether, only the supporting framework remaining, with many œdematous spaces in its meshes. The inner nuclear layer is reduced to a few scattered cells. Between it and the outer nuclear layer there are large spaces often containing coagula. The outer nuclear layer is on the whole well preserved, but where the changes are most advanced it shares in them. The rods and cones are fairly well preserved. There is sub-retinal and vitreous coagulum, but no recent hæmorrhage in either situation.

The cornea is normal. The anterior chamber is filled with coagulum. The iris shows extreme condensation of its stroma. There is a layer of new-formed connective tissue on its anterior surface, which, by its contraction, has greatly diminished the breadth of the iris, and has pulled the sphincter, and with it the uveal pigment, round anteriorly. There is a firm adhesion of the root of the iris to the back of the cornea. On the nasal side it measures 0·93 mm., on the temporal 1·71 mm. On the temporal side the iris is adherent in its whole breadth. The ciliary body and choroid are highly atrophic.

The case was a puzzling one clinically, inasmuch as, in spite of the extensive retinal hæmorrhages, the veins were small, not large and tortuous as is usual. This caused a very reasonable doubt as to the diagnosis. The case shows well the interaction of pathological states of the two sides of the intraocular vascular system, an interaction which should never be forgotten in considering the results of disease of the one or the other. It is most probable that the first lesion in this instance was the localised nodule of endarteritis at the lamina cribrosa. In consequence of this the intraocular circulation would be slowed, and thrombosis of the central vein in the usual situation would be favoured. This would cause the profuse retinal hæmorrhages. But

the heightened blood-pressure caused by the venous obstruction would evidently react unfavourably on the endarteritis, which would increase. Hence the arterial supply would be more and more interfered with until, when the lumen of the artery became quite filled up, it would be entirely cut off. The engorged veins would practically cease to be filled from the arterial side, while they would be drained to a certain extent by the small collaterals about the nerve head, and they would therefore become small and empty again. In addition, some of them were destroyed by thrombosis and organisation. I have already reported an instance of obliteration of the artery in a case of thrombosis of the central vein (Case 4 of my former paper), and I have also recorded a case in which there was reason to believe that the vein had become thrombosed secondarily to an obstruction of the artery.* Without doubt such cases have caused much confusion in the literature, and have led to the statement that intense hæmorrhagic retinitis may be due to disease confined to the arterial side of the circulation, a statement which, if true, would only lead to accumulated difficulties, and which I believe to be entirely erroneous. Harms has also reported similar cases, and comes to the same conclusion. The disease of the arteries is the indirect cause of the thrombosis of the central vein, but it is the thrombosis of the vein which is the cause of the clinical picture.

The case shows some points of resemblance to Cases 6 and 7 reported above, viz., the comparatively early age of the patient (34), and the occurrence of retinitis proliferans, and of a new-formed membrane on the anterior surface of the iris.

CASE 11.—*Thrombosis of the left central vein of two months' duration in a man, aged* 78. *Iritis. Glaucoma about nine days later. No improvement with treatment. Enucleation* $4\frac{1}{2}$ *months from onset of symptoms. Organising thrombus in*

* R. L. O. H. Rep., vol. xvi, pt. iii, Case 2, p. 227.

central vein some distance behind the lamina cribrosa. Corneo-iridic angle more occluded on the temporal than on the nasal side.

I am indebted to Mr. R. W. Doyne for the material and notes of this case:—

A man, aged 78, came to the Oxford Eye Hospital on December 20, 1904, complaining of failure of vision of the left eye of two months' duration. There had been no pain. The iris was discoloured, inactive, and bound down by a broad synechia below. V.R. with + 1·5 sph., 6/9. V.L. fingers at 12 inches. Tension of left perhaps slightly higher than that of right. With the ophthalmoscope, thrombosis of the central vein was diagnosed by Mr. Menteith Ogilvie. Nine days later the tension of the left was distinctly raised (+ 1), and the cornea hazy. *The anterior chamber was very deep.* The eye remained painful and injected. The pupillary edge became vascularised, and on January 26, 1905, a large hyphæma occurred. Signs of iritis with severe pain continued, the tension remained continuously high, and the eye was therefore excised on March 8, 1905.

The eye was bisected by Mr. Doyne, and the half of it containing the central vessels was sent to me for examination.

Pathological Examination.

The eye has been divided horizontally. The anterior chamber is of average depth; its angles seem to be occluded. The lens is *in situ.* The vitreous is absent. The retina is studded with hæmorrhages. The disc is not cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—The nerve entrance was accidentally cut longitudinally, a direction not well suited to the exact study of changes in the vessels and of their relations to one another. In the present instance, however, the obstruction happened to be found, and the case is reported as giving a good general view of a thrombus, and as furnishing a useful commentary on the cases already described.

The veins on the papilla are large and filled with normal blood corpuscles. They have normal walls. As the vessel is

passing through the lamina cribrosa the blood within it gives place to homogeneous coagulum, in which a few polymorphonuclear leucocytes are present (Plate VII, Fig. 18, A). Some distance behind the lamina other cells appear in the coagulum, with somewhat elongated pale nuclei; these form a knot, which for a short distance fully fills the lumen of the vein (B). It then begins to taper off and ends in a sharp point free within the lumen. A few blood corpuscles are present in the space between this conical mass and the vein wall. No collateral vessel is seen to enter the vein at the point where the obstruction ends, but, owing to the direction of section, one may easily have been overlooked. The vein remains perfectly patent from the point of obstruction to the cut surface of the nerve. There is nowhere any inflammatory infiltration of the surrounding connective tissues. The artery is normal throughout, the nerve is atrophic, and there is no glaucomatous cupping.

The cornea is normal. The iris is very atrophic and its root is firmly adherent to the back of the cornea on both sides, but much more extensively on the temporal. The measurements are—temporally, 1·60 mm.; nasally, 0·64 mm. The ciliary muscle is atrophic and flat, and the choroid is also atrophic. Both the retinal arteries and veins are thick walled, the process being one of fibrosis. Hæmorrhages are abundant, but usually not very large. The outer nuclear layer is best preserved; all layers internal to it are much scattered and destroyed; the nerve fibre and ganglion cell layers especially are very highly atrophic.

The case is useful, as showing in a single section points which have to be reconstructed from a series when the nerve is cut in the usual manner. It will be evident that a transverse section through the lamina cribrosa would give an appearance similar to Fig. 7 of my former paper; a section through the cellular knot would be similar to Figs. 3, 5, 7, 14, or 17 of the present paper; and one through the conical projection, to Fig. 6 of the former paper.

Remarks.

It may be useful to go over some of the points mentioned in my former paper, to see how far they should be modified in view of the larger material now at disposal. It would seem that the collection of more fully examined cases has tended to simplify the questions at issue. The cases given in this paper are not in any way picked, but include every instance in which a diagnosis of thrombosis of the central vein was made with the opthalmoscope, or, if the fundus had never been seen, by macroscopic inspection of the divided eye. In every one of them an obstruction was found in the vein which fully accounted for the symptoms. Harms also found an obstruction in the vein in every case in which he examined the whole course of it in transverse serial sections. Sidler Huguenin's and Baquis' are also cases in point. There can hardly be a doubt, therefore, that in all typical cases an obstruction would be found in some part of the central vein. If this be admitted, it at once clears away two of the six explanations which, as I stated in my former paper, have been advanced to explain the clinical picture, namely, (1) *multiple emboli or thrombi of the retinal arteries* and (2) *changes in the retinal vessels* (*hyalin thickening, endarteritis, and endophlebitis*) *not the result of either thrombosis or embolism.* Another explanation, *hæmorrhage into the substance of the nerve*, has never met with any proof since it was propounded by Deutschmann, and may probably be safely given up. *Multiple thrombi in the retinal, without thrombosis of the central vein* must be admitted to be theoretically possible, but it has so far not been shown to occur in a case in which the whole course of the vein was properly examined, though believed by Harms to be present in one of his cases in which the nerve was cut longitudinally. On the other hand, extensive thrombosis of the retinal veins has been found associated with proved thrombosis of the central vein. The former possibility must therefore be

accepted with all reserve until more definite proof is forthcoming.

Of all the explanations given, only two seem to have stood the test. *Primary disease of the vein wall* seems to have been clearly proved in one of Harms' cases and in Case 8 above. In the vast majority of cases, however, the lesion is a *thrombus* in a more or less advanced condition of organisation. This was found in 14 out of 16 of my own cases, and in 6 out of 7 of Harms', in which the obstruction was found with certainty. It may seem a small thing to be able to say that the clinical condition known as "thrombosis of the central vein" is indeed due to a thrombus in that vessel, but anyone who has read the recent literature of the subject will not consider it so.

While admitting that there are many gaps in our knowledge, an attempt may be made to sketch the pathological history of a case of thrombosis. There is a certain amount of evidence that the cause of thrombosis in the central vein may fall under one of two headings. In one set of cases there is no inflammation of the vein wall either at the point of thrombosis or elsewhere. Such cases usually occur in old people with extensive endarteritis of the central artery or its retinal branches. The thrombosis in this case is probably due chiefly to slowing of the current, assisted no doubt by some degenerative senile change in the endothelium of the vein. Exceptional instances of primary disease of the vein wall would fall under this class. Nephritis and possibly syphilis would be powerful predisposing causes, but are by no means necessarily, or even frequently, present. In the other class there is widespread round-cell infiltration of the vein wall, both in the nerve and in the retina. Such cases tend to occur in younger people, and there is often a history of some general disease, such as gout, rheumatism, syphilis, sepsis, or influenza (see Cases 6 and 7). In my own experience a history of influenza is frequently given. Such cases are, perhaps, specially liable to the occurrence of retinitis proliferans. The second class probably furnishes most of

the patients who remain in good health years after the attack; those included in the first class will be liable to various accidents. While, however, it is possible to cite typical cases in each class, it is doubtful how far they are practically separable in every instance, and at any rate they will not be mutually exclusive. When thrombosis has occurred there seems to be no difference in the prognosis with regard to the eye in the two classes.

Whether due to slowing of the current or to primary inflammation of the wall, the thrombosis is always deposited within or immediately behind the lamina cribrosa. I have discussed the reason for this in former papers. The first reaction on the part of the tissues seems to be a proliferation of the endothelium, which invades the clot from all sides (Figs. 1 and 16). Some authors hold that all the subsequent stages of organisation in small vessels, such as the central vein, proceed from this proliferated endothelium, but I believe the evidence rather favours the participation of the surrounding tissues. The comparatively small, darkly-stained, elongated cells which are found in cases with fairly advanced organisation, the indefiniteness of the outer boundaries of the cellular knot, and the total loss of the normal outline of the vein wall (Figs. 9, 11, 13), are all points in favour of organisation from the surrounding tissues, not from the endothelium of the vessel.

The subsequent steps vary in different cases. Most commonly the vein becomes greatly shrunken from the contraction of the organising tissue within it, and finally it may totally disappear over a certain area. In other rarer instances the organising material becomes canalised, new endothelium-lined channels burrow into it from the old lumen, and a considerable circulation may be restored. In any case the vein does not remain obliterated for more than a short distance. The thrombus only extends as far as the nearest collateral branch; if this happens to be large, a full lumen is restored at once, if small, this only occurs gradually from the entrance of other collateral branches. If a

sufficiently long piece of nerve has been excised, the lumen will always be found to be restored before the point of exit of the vein.

It is easy to understand why the retinal hæmorrhages and enlargement of vessels follow occlusion of the central vein. The occurrence of glaucoma is a much more difficult problem. I have already discussed this subject in my former paper, and have little to add. The present series fully confirms the statement, that even in early cases vitreous hæmorrhages are not present. In recent cases also the corneo-iridic angle is already found occluded, but often only slightly, and the extent of the adhesion bears a rough relation to the duration of the glaucoma. I still consider the most probable explanation to be the more albuminous nature of fluids the of the vitreous, and therefore of the aqueous, due to the venous obstruction and retinal hæmorrhages behind. But this explanation is not altogether satisfactory, for it does not easily account for the occlusion of the angle by *adhesion* of the iris to the back of the cornea—an adhesion around which there are no inflammatory infiltrates in recent cases. In the somewhat similar case of serous iritis, where the increased tension, when present, is probably also due to an alteration of the fluids to be drained off, the angles are not usually found occluded by adhesion. On the whole, therefore, it must be confessed that a fully satisfactory hypothesis has not yet been advanced to account for the glaucoma. It is hardly conceivable that it is due to the damming back of the small quantity of lymph which normally leaves the eye by the posterior perivascular lymph sheaths.

It is apparently not due to the carrying forward of the lens and iris, since, as has been repeatedly mentioned, the anterior chamber is usually of normal depth, or at least much less shallow than in primary glaucoma. In this point there is a certain agreement with serous iritis, except that in the latter the anterior chamber is not merely normal, but is increased in depth. I have already shown the clinical importance of this depth of the anterior chamber. When

there is a history of loss of vision without pain, and when pain and glaucomatous symptoms have come on subsequently, the other eye remaining normal and with a full field, the diagnosis probably lies between thrombosis of the central vein and intraocular tumour, provided that the glaucoma is not obviously secondary to iritis, etc. If now the anterior chamber is found to be of normal depth, the probabilities are in favour of thrombosis of the central vein, if shallow, in favour of intraocular growth. Unfortunately the value of the distinction is somewhat lessened by the fact that if glaucoma has ensued on thrombosis of the central vein, it is nearly as hopeless to save the eye as in the case of a tumour, but at least the case is not so urgent, and the attempt may be made. The measurements given in the pathological examinations seem to show that the lens is not unduly large in these cases.

I have several times pointed out the curious fact that in cases of glaucoma following upon thrombosis, the corneo-iridic angle is often much more widely occluded on the temporal than on the nasal side. In 11 cases in which the globe was bisected horizontally this was found 9 times. In one of those in which it was not found an iridectomy had been performed. The greater occlusion on the temporal than on the nasal side does not seem to be due to any anatomical difference, as I was unable to detect any in a normal globe; in especial there was no difference in the average thickness of the ciliary body or height of the ciliary processes in a number of serial sections taken through the middle of the pupil. In order to find whether or not this is the rule in other forms of glaucoma, I examined some other glaucomatous eyes. Unfortunately it is the custom, where no reason to the contrary exists, to divide globes sagitally. Moreover, in many of those divided horizontally the glaucoma was secondary to wounds, and was therefore not strictly comparable with that under consideration. It is also unusual to obtain other forms of glaucoma in an early stage and uninterfered with by opera-

tion. I was therefore only able to find six which were suitable for purposes of comparison. In four of these the angle was equally occluded on both sides (two cases of sarcoma of the choroid, one of buphthalmia, one of old injury). In one the angle was slightly more occluded on the nasal than on the temporal side (case of ? primary glaucoma in a diabetic), and in one slightly more on the temporal than on the nasal (old primary glaucoma). It is possible therefore that this is a peculiarity of the glaucoma following upon hæmorrhagic retinitis, but as I am unable to offer the least explanation of it, I must be content to simply record the observation, leaving its explanation to future research.

I have endeavoured to obtain particulars as to the subsequent course of thrombosis cases. For this purpose I have made use of the cases already published by me, those cases reported in the present paper (except three, which are too recent to be of value), and some cases from the practice of the hospital, all of which I have personally observed at one period or another. For the use of the notes of the latter I am indebted to Mr. Treacher Collins and to Mr. Percy Flemming.

This gives a material of 20 cases. Of these I have been unable to trace eight. Of the remaining 12 two died; Case 1 of my previous paper died in hospital of nephritis; Case 2, as Mr. Snell has kindly informed me, died suddenly, probably from cerebral apoplexy, four and a-half months after the first onset of symptoms. Before his death he had had severe headache and some mental symptoms, but no further attacks of loss of consciousness, etc., as described in the previous report. Another (Case 1 of the present paper) was in the last stages of chronic Bright's disease in March, 1906.

The following interesting history was obtained in a case seen five years previously:—A woman, aged 54, came to the hospital under Mr. Treacher Collins in April, 1901. She

had thrombosis of the right central vein. The urine contained no albumen or sugar. The day after she left hospital, according to a statement made by her husband, she had a "fit" and was unconscious for a whole day. She was an invalid for three or four months afterwards, but subsequently recovered sufficiently to go about fairly freely. During the ensuing two and a-half years she had occasional similar attacks of less severity. Two years ago she had a severe attack, and on recovering consciousness had right hemiplegia. This has never been fully recovered from, but it has not increased, although she has had several subsequent fits of unconsciousness. Her general health during the whole period has been fairly good. The vision of the right eye has remained practically unaltered since her first visit, that of the left has never been affected. This history would seem to point to thrombosis of cerebral vessels, the hemiplegia being due to thrombosis of the vessels supplying the internal capsule. This case, and the case of Mr. Snell, are the only instances which I have personally met with of cerebral symptoms associated with thrombosis of the central vein.

Another case was seen five years after thrombosis had been diagnosed. It concerned a woman aged 45, who was under the care of Mr. Treacher Collins in March, 1901. Thrombosis of the right central vein had been present probably for five weeks. There was no albumen or sugar in the urine. When seen in March, 1906, the veins were still very tortuous, but not enlarged. They were rather small and extremely sclerosed. The arteries were also small and accompanied with white lines. There were no hæmorrhages, but many large white patches all over the fundus, especially one extremely large and slightly raised patch upwards and inwards; in this patch there were some small curly new-formed vessels. Small nets had formed round the periphery of the disc, and its edges were hazy. The vision of this eye was 1/60, and it had not altered in the five years. The vision of the left was 6/6,

and with +2 D sph., J. 1. The left fundus was perfectly normal. Her general health had been good throughout the whole period. The tension was normal in both eyes.

The following case was watched for two and a half years. A woman, aged 42, was under the care of Mr. Treacher Collins in November, 1903. She had typical thrombosis of the central vein of the left eye. The urine contained no albumen or sugar. Her subsequent visits were irregular, but nine months later she came with the vitreous full of hæmorrhage. Two months later this had largely cleared up, and an exquisite retinitis proliferans was revealed, with much sclerosis of the retinal vessels. She was seen occasionally during the next 18 months. The retinitis proliferans altered very little, the connective tissue becoming rather more transparent, and allowing the vessels to be more clearly seen. The right eye remained normal throughout, except for a moderate degree of arteriosclerosis. The tension of both was normal. Her general health continued unimpaired.

In another case under the care of Mr. Flemming the fundus altered very little in two years. The veins remained very large and tortuous, white degenerative patches gradually appeared, and small nets formed in the periphery of the disc. No fresh hæmorrhages occurred; the other eye was healthy except for some arteriosclerosis; the tension of both was normal, and his general health had remained good. In this case there was a very faint trace of albumen in the urine on two different occasions. His peripheral arteries were also rigid, and his pulse of high tension.

Another case showed no alteration in four months, and a year later his medical attendant, Dr. A. K. Thomson, mentions nothing of an affection of the other eye, or of glaucoma in the diseased eye, in a note which he kindly sent me as to his condition. The urine contained a trace of albumen in this case, and the peripheral arteries were very rigid. He suffered much from bronchitis.

In the case in which expulsive hæmorrhage followed

upon iridectomy (Case 8) Mr. Flemming informs me that in March, 1906, there were no hæmorrhages in the other eye; the disc was pale, and both arteries and veins small. The urine contained no albumen or sugar.

A case of thrombosis of the superior temporal vein was watched for three and a half years, during which hæmorrhage occurred into the vitreous several times, but neither glaucoma nor retinitis proliferans ensued. This case could not be traced in March, 1906.

Two other patients were not seen, but wrote to say that they were in good health, and that the other eye had remained unaffected.

From a consideration of these cases the most important fact which emerges is the total immunity of the other eye. I have not personally seen or heard of a case in which it became affected, and the literature is almost equally silent on the subject. With the doubtful exception of v. Graefe, who wrote before this class of cases was well separated from other conditions of retinal hæmorrhage, and of Goh,* whose case was exceptional in many respects, no author seems to mention affection of the other eye. This is rather an unexpected fact in a condition which might be thought to depend chiefly on general angiosclerosis. It is, however, of great importance, since the patient may be assured almost with certainty that his remaining eye is safe.

The figures do not show in what proportion glaucoma follows upon thrombosis of the central vein, since the clinical cases in which glaucoma *did not* ensue were all gathered from two cliniques, whereas the pathological material in which it *did* ensue was collected from the whole practice of the hospital, as well as from private sources. The collection within a period of about three years of 16 cases in which glaucoma ensued, sufficiently shows that there must be some definite connection between

* In Goh's case hæmorrhages occurred in both eyes a few days before death from septic poisoning. A thrombus was found in the right central vein, not in the left (Arch. f. Ophth., vol. xlviii, pt. i, p. 147, 1897).

the two conditions. Indeed, it may be said that in any given case there is very considerable danger of the occurrence of glaucoma. It is, however, evident from the cases quoted above, that the condition may last for a period of years, and may be complicated with vitreous hæmorrhage *without* giving rise to glaucoma. One important clinical lesson to be drawn from this fact of a liability to glaucoma, is that, when a diagnosis of thrombosis has been made, no mydriatic should ever subsequently be employed—not even homatropine. In four out of 16 cases in which glaucoma followed, there were the strongest reasons to believe that it was directly precipitated by the use of a mydriatic (atropine twice, homatropine twice). In one of these it developed immediately, while the patient was waiting for ophthalmoscopic examination.

It does not appear from the above data that the occurrence of thrombosis gives much help in forming a prognosis as to the life of the patient. The prognosis does not seem to depend so much on the thrombosis *per se* as on the general health of the patient. Two of the cases died, but one of them had advanced Bright's disease, while the other had had an attack of apoplexy. Another case, which was *in extremis* when last heard of, was also the subject of advanced Bright's disease when first seen. In all these cases a bad prognosis would have been given quite independently of the thrombosis. On the other hand, we have cases watched for 5, $3\frac{1}{2}$, $2\frac{1}{2}$, $1\frac{1}{3}$, $1\frac{1}{4}$ years, without the least deterioration of their general health. In only two cases did symptoms of thrombosis elsewhere (in the brain) ensue. The numbers are, however, too few, and the cases are not yet sufficiently long under observation to allow of any very certain conclusion being drawn.

Description of Plates IV to VII, Figs. 1 to 18.

In all the photographs in which both vessels are shown the vein is above.

Fig. 1. × 120.—Central vein in anterior part of the lamina cribrosa in Case 1. It is obstructed by a mass which shows a reticular structure. No red corpuscles could be seen in it, but it contains polymorphonuclear leucocytes, and also larger paler cells, possibly derived from the endothelium. The original outline of the vein is distinct, and the mass has shrunk away from the wall. There is no round-cell infiltration of the surrounding tissues. The thrombosis is evidently not of long duration.

Fig. 2. × 120.—Termination of the thrombus immediately central to the lamina cribrosa in the same case. The lumen is restored by the accession of a large branch from the surrounding connective tissues. From this point onwards the lumen of the vein was normal.

Fig. 3. × 120.—The central vessels in Case 2. The lumen of the central vein (above) is greatly encroached upon by a cellular organised tissue, with a distinctly fibrous ground substance. The original vein wall can no longer be traced with certainty. From the appearance of this section alone it would be difficult to say whether the obstruction was due to endothelial proliferation or an organised thrombus, but the examination of the whole series made the latter more probable. A few sections farther up the nerve the vein became completely occluded for a short distance. The artery is normal and filled with blood.

Fig. 4. × 120.—Method of restoration of the lumen in the same case. The general form of the vein is restored, and its endothelium is present. The lumen is mostly filled with coagulum. Into this a collateral branch from the surrounding connective tissues plunges, carrying with it a stream of normal red blood corpuscles. From this point backwards the vein was normal, and its lumen contained blood.

Fig. 5. × 120.—The central vessels from Case 3. The vein contains a thrombus, in which the process of organisation is more advanced than in the last instance. The ground substance is more definitely fibrous, and the mass is more cellular and shrunken. It has shrunk away from the surrounding connective tissues—probably artificially. It is situated at the posterior level of the lamina cribrosa. The artery is somewhat collapsed, but shows no endarteritis. In this case only a short piece of nerve was excised with the globe, and the vein had not recovered a lumen before it reached the cut end of the nerve.

Fig. 6. × 170.—A retinal vein from the same case. It is occluded by a completely organised thrombus. There is a considerable collection of pigment granules (blood pigment) round it. Note the comparatively good preservation of the outer nuclear layer, with almost total atrophy of the layers internal to it.

Fig. 7. × 120.—The central vessels in Case 4. The position of the vein is shown by the letter A. This section is towards the posterior level

of the lamina cribrosa. A short distance further forward the shrinkage of the vein was still more extreme. In the section shown there is a small shrunken coagulum in which a few red corpuscles could be seen with higher powers. There is a distinct round-cell infiltration of the surrounding connective tissues at one side. The artery is obliquely cut at this level, and does not show well the changes described in the text.

FIG. 8. × 120. The central vessels from Case 5. The section shown is from the anterior part of the lamina cribrosa. The outline of the vein is distinct, but its lumen is occluded by an almost homogeneous mass, in which a few leucocytes and other cells are present. In the artery the elastic membrane has separated from the media, presumably artificially. Within it there is a mass of detritus formed by the breaking down of the large vacuolated cells (see also Fig. 10 and description of Case 4 in the text). Within this again there is a single layer of endothelium resting on a kind of basement membrane. The lumen is exceedingly small and eccentrically placed. The appearances are probably not due to proliferation of the endothelium, which remains as a single layer lining the lumen, but to proliferation of the cells of the normally very thin layer of subendothelial tissue lying between the endothelium and the elastica.

FIG. 9. × 120.—Section still within the lamina cribrosa from the same case. The vein is entirely obliterated, its position being marked only by a more cellular knot in which the nuclei are mostly oval (A). The artery shows the same changes as in the last figure. Note the density of the connective tissue around the central vessels as compared with the next figure. This is always found at the lamina cribrosa, and may have some importance in determining the frequency of vascular disease there.

FIG. 10. × 120.—Section from the same case further back. A small lumen has been restored in the vein, but its walls are extremely thick and infiltrated. The artery shows better than in the preceding photograph the cellular character of the tissue from which the detritus found more anteriorly is formed. Some of these cells are very large and contain more than one nucleus—resemble, in fact, small giant cells. The single-layered unaltered endothelium is well seen.

FIG. 11. × 120.—The central vessels from Case 6. The section is from the posterior part of the lamina cribrosa. The lumen of the vein is encroached upon from one side by a conical mass. There is much round-cell infiltration both in the mass and in the surrounding connective tissues on the side from which it springs. Nearer the surface of the papilla the vein was completely obliterated, and its position indistinguishable; further up the nerve its lumen was speedily restored. The artery is somewhat obliquely cut, but has normal walls.

FIG. 12. × 120.—A retinal vein from the same case, showing an unusual amount of round-cell infiltration in its wall. This, and the thrombus in the central vein were probably associated with an attack of influenza, during which the sight of the eye was lost.

FIG. 13. ×120.—The central vessels in Case 7. The section is from the posterior part of the lamina. A normal and patent vein was present in front of this level. The outline of the vessel cannot be traced. Its position is occupied by an area of highly cellular tissue, in which three small lumina are present, each lined with endothelium and containing homogeneous coagulum, but no corpuscles. In the section immediately in front of this level the same cellular tissue was present but without the lumina. The condition probably represents an early and incomplete stage of canalisation. The obstruction of the vein is only present over a very small area. The lumen was restored a few sections up the nerve and remained patent.

FIG. 14. ×120.—The central vessels in Case 8. The level of the section is immediately posterior to the lamina. The vein is completely occluded by a loose cellular mass, somewhat similar to that shown in Fig. 1, but rather more advanced in organisation. There is no surrounding round-cell infiltration. The artery has normal walls, and is filled with blood.

FIG. 15. ×120.—The central vessels in Case 9. The section is from a point somewhat behind the posterior surface of the lamina. The obstruction in the vein differs from that shown in previous figures in having a definite concentric arrangement both of its fibres and nuclei. There is also a small central lumen containing coagulum and blood. In sections farther up the nerve this was still more reduced in size so as to be of practically capillary dimensions. The mass has shrunk away from the wall—probably artificially. The case is probably one of endothelial proliferation. The artery is normal, and contains a little coagulum.

FIG. 16. ×120.—The central vessels in Case 10. The section is within the lamina cribrosa. The vein is of full size and somewhat enlarged. Its lumen is occupied by granular detritus, in which a few broken-down red corpuscles are visible. There is also a delicate reticulum with some large, pale, probably endothelial, cells in its meshes. The artery is much shrunken and completely occluded by endarteritis.

FIG. 17. ×120.—A section behind the lamina from the same case. The vein is much smaller, but still not greatly shrunken. It is occupied by a fully organised mass of tissue. There is no surrounding cell infiltration. The lumen of the artery has become patent. It is only slightly narrowed by endarteritis at one side. The endothelium is preserved.

FIG. 18. ×120.—A longitudinal section through the nerve in Case 11. From the region of the lamina cribrosa (A) backwards the vein is occupied by a homogeneous coagulum. There is slight endothelial proliferation. Some distance behind the lamina (B) the coagulum becomes invaded by cells—polymorphonuclear leucocytes and larger paler cells. The obstruction ends in a pointed extremity, which is free in the centre of the lumen. The vein wall is normal above this point, and there is nowhere any round-cell infiltration of the surrounding tissues. The artery is not present in this section.

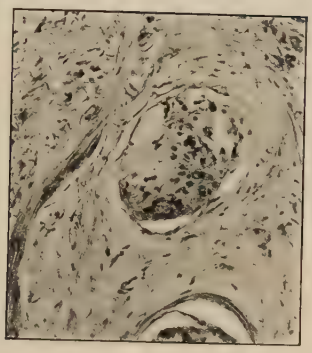


FIG. 1.

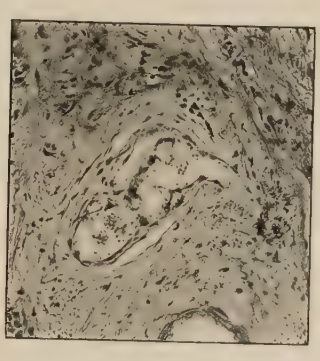


FIG. 2.

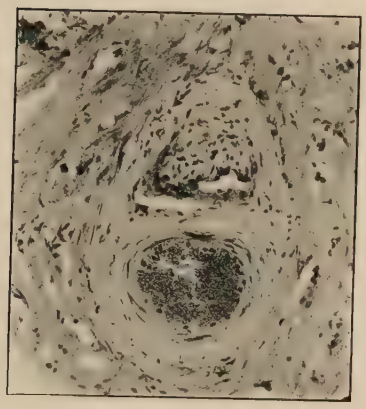


FIG. 3.

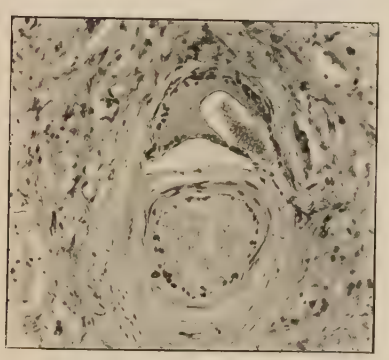


FIG. 4.

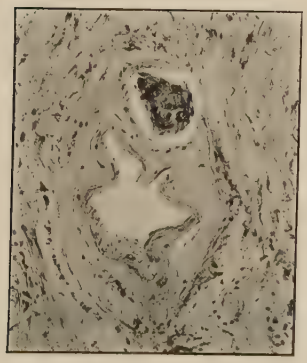


FIG. 5.

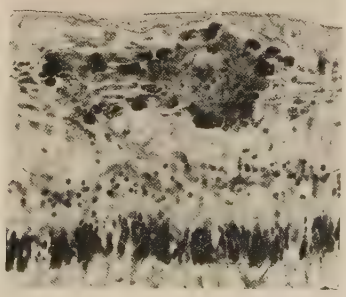


FIG. 6.

Bale & Danielsson, Ltd.

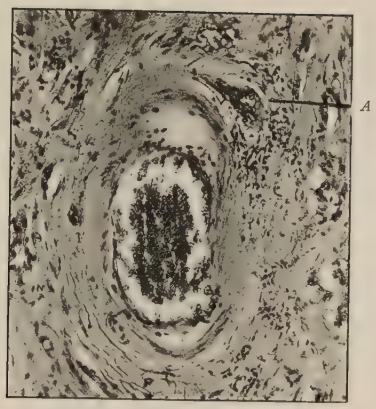


FIG. 7.

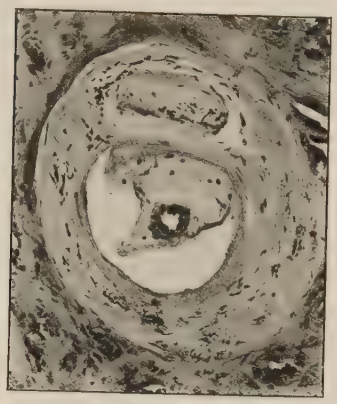


FIG. 8.

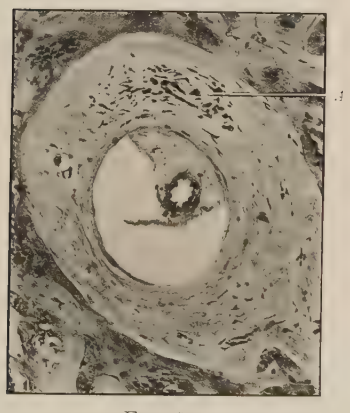


FIG. 9.

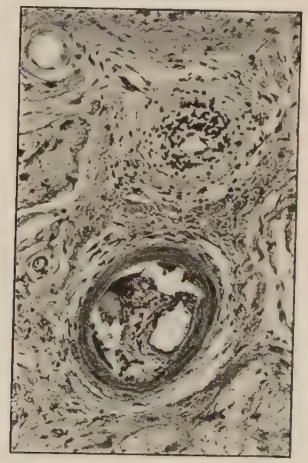
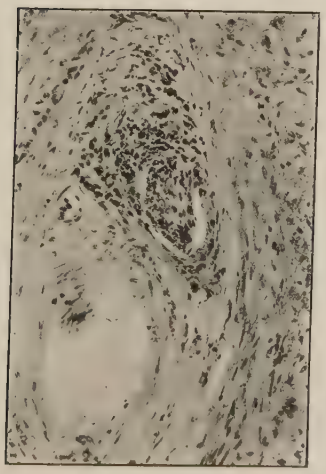


FIG. 10.



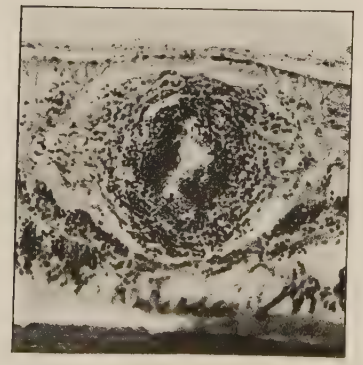


FIG. 13.

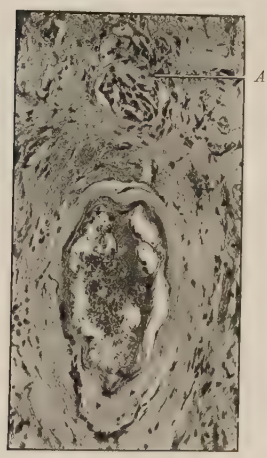


FIG. 14.

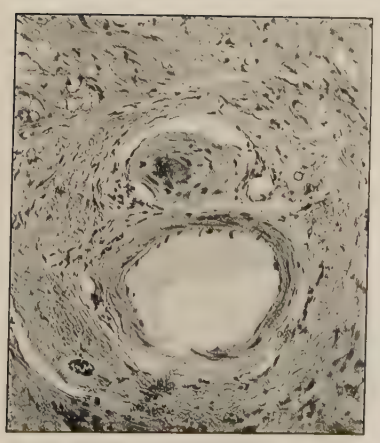


FIG. 15.

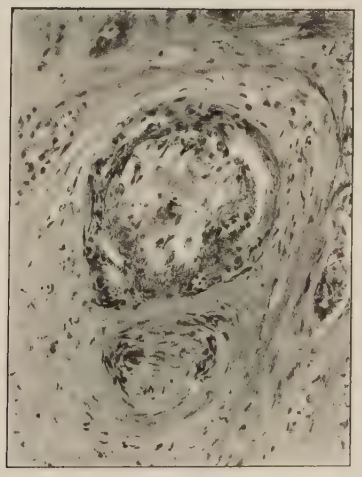


FIG. 16.

Bale & Danielsson, Ltd.

ON METASTATIC INFECTION OF THE EYE ASSOCIATED WITH (*a*) CEREBRO-SPINAL MENINGITIS; (*b*) TYPHOID FEVER.

From the Andrew Clark Laboratories, London Hospital.)

By M. S. Mayou.

Cases of definite endogenous infection of the globe are comparatively rare. The two cases described below show very well the early and late stages of the disease. The first case, which was associated with cerebro-spinal meningitis, was of 24 hours' duration, whilst the second had lasted several days. In both cases the specific micro-organism was found in the globe in the pure state.

(*a*) Cases of endogenous infection of the eye associated with cerebro-spinal meningitis which have been previously reported, have all been cases in which the disease in the eye had lasted for some time, and had led to the condition known as pseudo-glioma. Further, in those cases which have been recorded by Cross [1], Nettleship [2], Collins [3], Stephenson [4], Flemming [5], and Axenfeld [6], the specific micro-organism was not demonstrated in the globe; the inflammatory process was said to have travelled to the globe *viâ* the optic nerve and sheath, those structures being found to be inflamed. In the case about to be described the infection of the eye was undoubtedly metastatic.

Case 1.—A. L., male, æt. 3. Admitted to the London Hospital, under Dr. Head, November 1, 1905; died November 3.

History of the Onset.—Had been ill only since the morning. Did not take food well the day before, but ran about as usual. In afternoon complained of being tired. Restless all night. At 5.30 A.M. kept crying for water and was very hot. Went to doctor in the morning and was given medicine. Sick once after

first dose. Had not known mother since breakfast. Much screaming. Had much shaking in the arms. A fixed look in the eyes.

Previous Health.—Very good. One other child alive. One died of "twisted gut." No one else ill in the house.

Condition on Admission.—The fontanelles were still patent. Heart *nil.* Lungs clear. Abdomen *nil.* Child lay on back or preferably (apparently) on right side. Eyes half open and staring. Slight rigidity of the neck, with retraction. Took no notice of lights or moving objects. Did not blink when hand was moved in front of the eyes suddenly. Frequently put hands up to head as though in pain; mostly, perhaps, the right hand to right ear. Occasionally there was a coarse shiver or clonic spasm of the arms, which always came on if child was roused. He screamed if disturbed at all, and was rather irritable, but appeared unconscious of what was going on around him. The lower limbs were somewhat spastic. There was no discharge from ears, and never had been any. No rash. No coryza. Tonsils large, no membrane.

Ears: Right drum: malleus red, drum somewhat indrawn, no bulging. Left drum: normal, rather indrawn.

Eyes: Discs clear. Pupils large when child was roused, equal, and reacted. Fundi, well marked retinal reflex.

November 2.—Child had a restless night. Temperature steadily rose until, at 8 A.M., it was 104°. Pulse ran up to 160, and respiration to 58. The child suffered frequently from "shaking fits"; both hands were affected, but the right mostly. Left hand, (?) paresis. During the night the child kept putting the right hand up to the right ear and side of head.

Eyes: Slight divergent squint at times; eyes moved asymmetrically. Right pupil was smaller than left, but they often varied. Fundi clear. Vessels seemed large.

Ears: Left drum had a whitish plaque in the centre, just below handle of malleus, and was indrawn. Punctured, no fluid whatever in middle ear.

Breathing rapid, no difficulty. Tonsils very large, red, inflamed, no membrane. Tongue very thickly furred. No rash. Fontanelle pulsating.

November 3.—Left lung a little dull, crepitations and râles,

(?) pneumonia. Respirations and pulse very rapid. Temperature, 104°. Child worse. Sweating. Not so cyanosed.

Eyes.—Large hypopyon was present in the right eye at 8.15 A.M., which had developed during the night. No red reflex was obtained. Anterior surface of lens covered with lymph. Eye a little congested. No wound of cornea or other part of eye.

More râles in the chest. Hypostatic œdema and collapse. Right lung most affected, left to some extent.

At 2.30 patient was very ill and obviously dying. Respirations had become slow. Pulse very rapid and weak. Cyanosis less marked, giving way to a dusky pallor. Right eye as before. No red reflex in spite of dilatation by homatropine. Left pupil dilated. Vessels quite clear. Veins rather large and congested. Disc clear (seen five minutes before death). No further signs. Died 2.45 P.M.

Post-mortem.—Body weight, 20 lbs. 8 ozs. Much P.M. staining, back, neck, and thighs. Hypopyon, right anterior chamber.

Pleuræ: No fluid, no adhesions.

Lungs: Surface mottled, showing areas of collapse in upper lobes. Lower lobes deep red in colour, slightly aërated, exuded fluid on pressure. Pieces did not sink in water.

Larynx: Healthy. Bronchi and trachea injected throughout. Heart: 3 ozs.; left ventricle firmly contracted. Right ventricle contained white clot. Ventricles not contracted. Muscles soft, deep red. All valves quite healthy.

Vessels: Healthy.

Abdomen: Stomach and intestines healthy. Peyer's patches slightly congested. Appendix healthy. No excess of fluid.

Spleen: 2½ ozs. Deep red, capsule smooth. Soft. Malpighian corpuscles prominent.

Right kidney: 2½ ozs. Pale, smooth, capsule stripped readily. Demarcation good. No diminution of cortex, which was striated with parallel lines of injected vessels.

Left kidney: Suprarenal vessels healthy.

Genito-urinary system: Bladder healthy.

Liver: 1 lb. 5 ozs. Pale, smooth, not soft. Healthy. Gall bladder full of bile.

Alimentary canal: healthy.

Brain: 3 lbs. The surface of the brain was redder than usual,

owing to congestion of vessels. The sulci contained a small amount of thin yellow pus lying in arachnoid space. Smears showed *Diplococcus meningitidis* in small numbers. No excess of fluid in ventricles and substance of brain, and on section appeared normal.

Spinal cord: Had lost its translucent appearance and looked somewhat greenish. The dura was coated with a thin layer of exudation which could be scraped off. The nerve roots were matted as they passed out through the membrane.

Right eye: Was removed and reserved for further examination. The optic nerve appeared normal to the naked eye.

Ears: No pus in middle ears.

The eye was hardened in formol and divided horizontally. The optic nerve, having been previously removed, was cut transversely in serial section.

The *retina* and *optic nerve* were normal. There was no distension of the nerve sheath or swelling of the nerve head.

The *vitreous* was clear except near the lens, where it was slightly cloudy.

The *lens* was in its normal position and there was no evidence of any injury to any part of the globe.

The *anterior chamber* contained a considerable amount of pus, shrunken and adherent to the back of the cornea, iris, and anterior capsule of the lens. Smear preparations of the pus showed enormous numbers of diplococci which were not stained by Gram's method, and were similar in appearance to those found on the surface of the meninges; unfortunately no culture could be made, as the specimen had been placed in formol, but they were evidently the *Diplococcus meningitidis*. The organisms were so numerous in the smear as to appear more like a culture preparation than pus from the body.

The eye was embedded in celloidin and paraffin, and the optic nerve, which had been previously removed, was cut transversely in paraffin. The optic nerve and central vessels were normal, there was no leucocytosis into it or its sheath, and no organisms could be found in sections stained with methylene blue.

The *retina*, *choroid*, and vessels were normal as far forward as the ora serrata.

The *lens* was normal. Around the *ciliary body* and entangled in the suspensory ligament of the lens and also in the region of the ora serrata was a large exudation of polymorphonuclear leucocytes. These pus cells were also found in the anterior chamber, especially at the lower angle. They were also found adherent to Descemet's membrane in the other parts of the cornea. The central and upper parts of the substantia propria were free from polymorphonuclear leucocytes, but below in the region of the Canal of Schlemm, and spreading inwards on the outer surface of Descemet's membrane, were a number of these cells.

The *iris* in its upper part was free from leucocytes, and there was no evidence of post. synechiæ. Below, near the angle, the iris was packed with polymorphonuclear cells.

The condition, therefore, is one of very early panophthalmitis starting in the ciliary region. Considerable controversy has arisen as to whether the infection of the globe in these cases is due to the direct extension of the inflammation down the nerve sheath or to embolic infection. In this case, in which the fundus was seen immediately before the onset of infection, and death took place within 24 hours after the fundus was examined, the posterior part of the globe, nerve and nerve sheath were found to be perfectly healthy on microscopic examination ; we have, therefore, positive proof that the infection did not take place by direct spreading from the meninges, and therefore infection must have taken place through the blood stream. The exact situation of the embolus was not discovered, but was evidently in the ciliary body, since polymorphonuclear leucocytes were most numerous in that region. The infiltration of pus cells in the neighbourhood of the Canal of Schlemm is of interest in that, as will be seen in the second case, a ring ulcer formed in that situation which subsequently caused necrosis of the cornea.

(*b*) Judging by the literature, cases of panophthalmitis in typhoid fever seem very rare, but perhaps this is owing to their not being reported, since they were noted as early as

1826, but at that date the differential diagnosis between typhus and typhoid fever had not been established.

A case, starting in a similar manner to the one about to be described, is reported by de Schweinitz [7], the only difference being that in his case there had been no previous inflammation in the eye.

Case 2.—H. R., male, æt. 22 ; an engineer's fitter. Attended the out-patients' department of Moorfields Hospital on June 20, 1899, under Mr. Tweedy, with double iridocyclitis. He attended again on October 6, 1899, when he was admitted as an in-patient. The following was his condition at the time of admission :—He was a strong, healthy man, and had previously been in the Navy. There was no history of syphilis or other trouble. Urine, Sp. G. 1028, no albumen or sugar ; his temperature was 99°. He was suffering from double iridocyclitis.

L. eye. The fundus could be seen, and there was a small retinal hæmorrhage. V. 6/60 Tn.

R. eye. Chronic iritis with partly occluded pupil ; some retinal hæmorrhage. T + 1. Bare P. of L.

On October 16, paracentesis on the right eye was performed, that is to say, ten days after admission. The same day his temperature rose to 104°, and some crepitations were heard at the bases of both lungs. Two days previous to this he had complained of severe headache. The right eye was much improved ; there was slight ciliary injection, the anterior chamber was deep, the wound healed well, and there was no pain.

As his general condition did not improve, on October 21 he was transferred to the London Hospital under Sir Stephen Mackenzie. On admission his temperature was 103° to 106° ; pulse 140, sordes of mouth, few râles in chest, and pains in the left side of the abdomen. The spleen was enlarged, typhoid spots were present, and Vidal's reaction was positive. On October 25 some œdema of the right conjunctiva was noticed, which rapidly increased during the next three days. There was no note of any hypopyon. The patient did not complain of any pain.

On October 29, under chloroform, the right eye was excised by Mr. Roxburgh with much difficulty and considerable

hæmorrhage. The patient made a good recovery from the operation. On November 8 a quantity of fluid was withdrawn from the left pleura. Subsequently the patient made a good recovery and remains well up to the present time, the sight of the left eye being in much the same condition as when he attended Moorfields.

Histological Examination.—The globe was hardened in formol and bisected horizontally.

The anterior chamber was filled with a tough fibrinous exudation, the root of the iris being pushed forward against the posterior surface of the cornea, occluding the angle of the chamber. The anterior chamber contained comparatively few pus cells.

The *lens* and *suspensory ligament* were intact.

The *vitreous* chamber was filled with reddish-brown pus. Smear preparations of the contents showed a large number of bacilli staining with methylene blue, but not by Gram's method, and although cultures could not be made owing to the specimen having been immersed in formol, the organism was probably the *Bacillus typhosus.*

The pus had made its way through the choroid about the equator, and through the sclera, just behind the insertion of the internal rectus muscle, forming an abscess beneath it.

The *cornea* was necrotic. The epithelium had disappeared from the surface. The substantia propria in the centre was comparatively free from pus cells, whilst round the margin a ring ulcer had formed which, towards the outer side, had caused complete perforation of the cornea, but on the inner side Descemet's membrane was still intact. (The early stages of this condition are well seen in Case 1.)

The *iris* and *ciliary body* were infiltrated with pus cells.

The *retina* had completely disappeared.

The *choroidal vessels* in the posterior part of the globe were converted into large venous sinuses which were enormously engorged with blood, whilst anteriorly the choroid was thin and atrophic ; equatorially in some situations it had disappeared altogether.

The facts that the wound from the paracentesis had

healed perfectly before there were any signs of inflammation, which clinically did not start in the anterior part of the eye; that the inflammation did not come till nine days after the operation, and that the vitreous chamber was full of pus, whilst the anterior chamber was comparatively free and only contained the fibrous membrane as the result of the old exudation, indicate that the infection must have taken place from within. The fact that a bacillus having the same characteristics as the *Bacillus typhosus* was found, together with the fact that the patient had other metastatic symptoms, *e.g.*, pleurisy, make it practically certain that the case was one of endogenous infection due to the *Bacillus typhosus* grafted on to an old chronic cyclitis of unknown origin.

For the use of the notes on the first case I am indebted to Mr. Lister and Dr. Head; for the notes of the second case to Mr. Tweedy, Mr. Roxburgh, and Sir Stephen Mackenzie; for the photographs of the micro-organisms to Mr. Henderson, and to Mr. Coats for the use of the Moorfields Hospital camera.

References.

1. Cross, F. R. Trans. Ophth. Soc., March, 1900, vol. xx, p. 117.
2. Nettleship. Trans. Ophth. Soc., 1900.
3. Collins, E. T. R. L. O. H. Rep., vol. xiii.
4. Stephenson. Trans. Ophth. Soc., June, 1900, vol. xx.
5. Flemming, P. Trans. Ophth. Soc., vol. xx, p. 130.
6. Axenfeld. Graef. Arch., Bd. xlii, 1896, p. 101.
7. De Schweinitz, G. Keen's Surgical Complications of Typhoid Fever, p. 304.

Description of Plates VIII and IX, Figs. 1 to 4.

Fig. 1.—Smear preparation of the pus from the anterior chamber of Case 1, showing the *Diplococcus meningitidis*. Stain—carbol-fuchsin. (Photo, E. E. Henderson.)

Fig. 2.—The lower angle of the anterior chamber (Case 1) showing the polymorphonuclear leucocytes in the iris and angle of the chamber. Note also the exudation in the neighbourhood of the canal of Schlemm

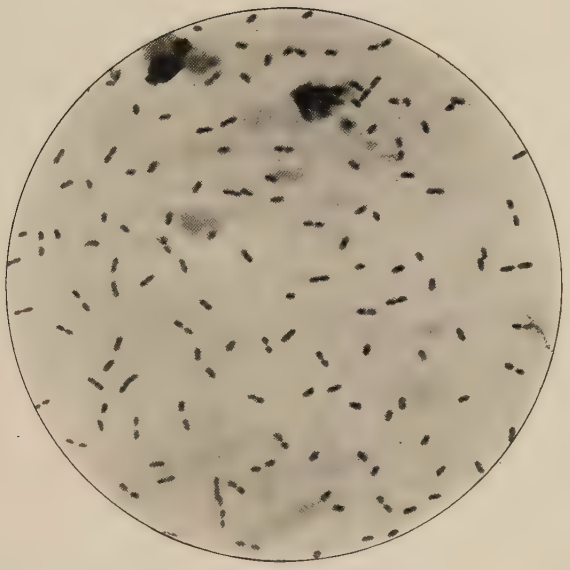


FIG. 1.

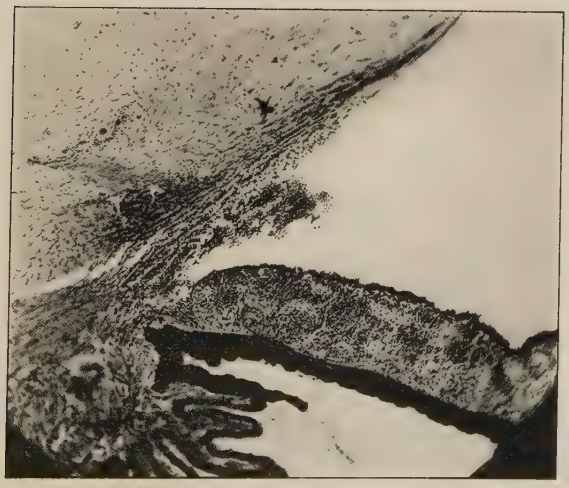


FIG. 2.

Bale & Danielsson, Ltd.

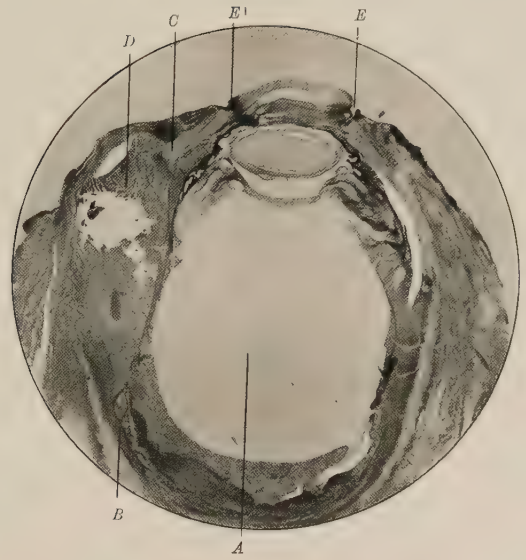


FIG. 3.

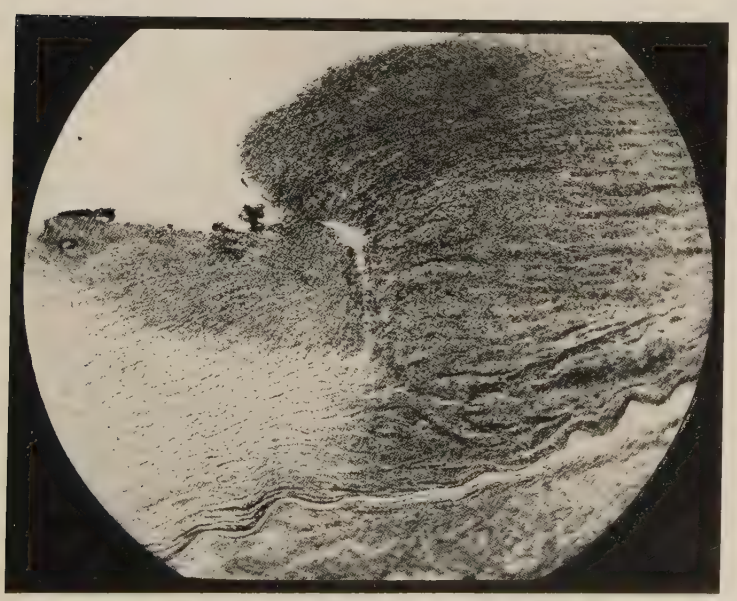


FIG. 4.

Bale & Danielsson, Ltd.

(early stage of the condition seen in Fig. 4). In the region of the ora serrata there was also a large collection of pus cells. The posterior part of the globe and the optic nerve were normal.

FIG. 3.—Horizontal section through the globe (Case 2). (A) The whole vitreous chamber was filled with pus, but is not shown in the section owing to the shrinkage brought about by the alcohol. (B) The choroidal vessels are enormously dilated at the posterior pole. The pus has ruptured through the choroid and sclerotic (C), and has formed an abscess beneath the tendon of the internal rectus (D). The anterior chamber is filled with old fibrinous exudate, in which there are comparatively few pus cells (E, E′). The ring ulcer which has formed round the cornea was perforated on the outer side.

FIG. 4.—Section through the ring ulcer towards the inner side (E′, Fig. 3) showing the necrotic cornea comparatively free from leucocytes. Descemet's membrane is still intact.

RETINA IN GLAUCOMA CUP.

By Malcolm Langton Hepburn, F.R.C.S.

To find retina or retinal elements in a glaucoma cup is extremely rare, and the cases described by Kampherstein [6] and Parsons [8] are probably unique. The question, therefore, naturally suggests itself as to how it came to be situated in this position.

I am inclined to regard it merely as a final stage in a series of changes produced in certain eyes which eventually become the subjects of glaucoma.

Although portions of retina are not often found actually inside a glaucoma cup, yet to find pathologically the excavation filled in with fibrous tissue is by no means so uncommon. Several cases have been described by Schnabel [1], Axenfeld [2], Krukenberg [3], Gama Pinto [5], Ginsberg [7], and Roscher [4], and I have collected together 30 similar cases from the pathological records of the hospital during the last four years; and it is the subsequent behaviour of this fibrous tissue which determines the character of the contents of the glaucoma cup.

There has been a good deal of discussion amongst the various writers, not only as to the origin of the contents of the cup, but also as to whether the glaucoma or the fibrous tissue existed first; and the cases have sometimes been described as "Glaucomatous excavation of the lamina cribrosa without excavation of the Optic Nerve." The explanation given by Axenfeld [2] and Krukenberg [3] is that some severe inflammatory condition of the papilla was present first and the glaucoma followed later. Other theories put forward by Krukenberg are that either there was a congenital excavation of the lamina cribrosa, into which some subsequent infiltration entered, or that a papillary neuritis takes place at the bottom of an old glaucomatous cup. Roscher [4], Gama Pinto, and

Ginsberg [7] favour the latter view; but the clinical evidence is not very convincing, since Roscher's case is that of a woman, aged 25, who had suffered from what was probably interstitial keratitis 10 years before, a history which hardly encourages a theory of primary glaucoma. To me it seems unlikely that an acute neuritis should take place in structures which have actually been atrophic for a long time, though Schnabel describes a case of optic neuritis, developing in an old glaucomatous eye, as a result of cerebral tumour. In a certain number of cases passive exudation does take place into a pre-existing glaucoma cup, probably as a result of acute inflammation of the ciliary body; and under these circumstances it is conceivable that subsequent organisation and contraction of the fibrous tissue might draw down some portions of retina near the cup; but by far the larger majority of the eyes examined are the subjects of secondary glaucoma, that is, secondary to some injury, operation, or inflammatory condition involving the cornea, iris, and ciliary body, thus leading to long-standing iridocyclitis, the evidences of which have always been found pathologically.

According to the extent and duration of these inflammatory processes, so we find various changes produced in the different structures, and the combined influence of chronic inflammation and degeneration produces such conditions as folded retina (Paton [10] and Parsons [11]), hyaline degeneration, retinal degeneration, etc., which are often most marked near the optic disc. Moreover, the formation and proliferation of fibrous tissue in the neighbourhood of the disc in connection with the central blood vessels, where there is most mesoblastic tissue (Parsons [9]), is commonly met with clinically, and in an extreme form as retinitis proliferans; but if these changes occur simultaneously with the inflammation elsewhere, strands of connective tissue spread out in the form of wings and attach themselves ultimately to surrounding structures, as shown in Figs. 1 (A) and 2 (D). Kampherstein also suggests the formation of fibrous tissue as a result of proliferation rather than of organised exudate.

Sooner or later an attack of glaucoma comes on, evidenced by pain and increased tension. The thrusting back of the lamina cribrosa produces stretching out of the fibrous tissue formed on the disc, and large spaces may result, as shown in Figs. 1 (B) and Fig. 3, which are very likely to become filled with blood or hyaline material. In other cases the fibrous attachment to the lamina cribrosa and surrounding structures is so firm that the parts adjacent to the disc are dragged upon, and thus we find degenerated retina, folded retina, etc., eventually settled in the excavation. In Parsons' case, a large mass of fibrous tissue on one side of the glaucoma cup indicates how the retina has been dragged over, and many of the specimens I have collected show the pulling on the retina in the earlier stages.

In the majority of cases, however, the retina does not hold, and we get the appearance seen in Fig. 4, where the retinal tissue is only united by a very fine strand (C), which would probably soon have given way, leaving a free end with its base attached to the bottom of the cup, Fig. 3 (D); quite a large number of cases can be seen in which this has occurred. I am very much indebted to Mr. Coats for his assistance in taking photographs of the sections, and for giving me every facility in getting the specimens together.

In the accompanying list of cases there are 30 in which definite fibrous tissue appears in the glaucomatous excavation, and out of this collection Nos. 12, 22, 30, and 32 represent Figs. 1, 2, 3, and 4 respectively. It has not always been possible to determine in each case when the glaucoma first appeared, as the date of onset has not always been recorded, but I have considered the occurrence of severe pain as indicative of the commencement of increased tension.

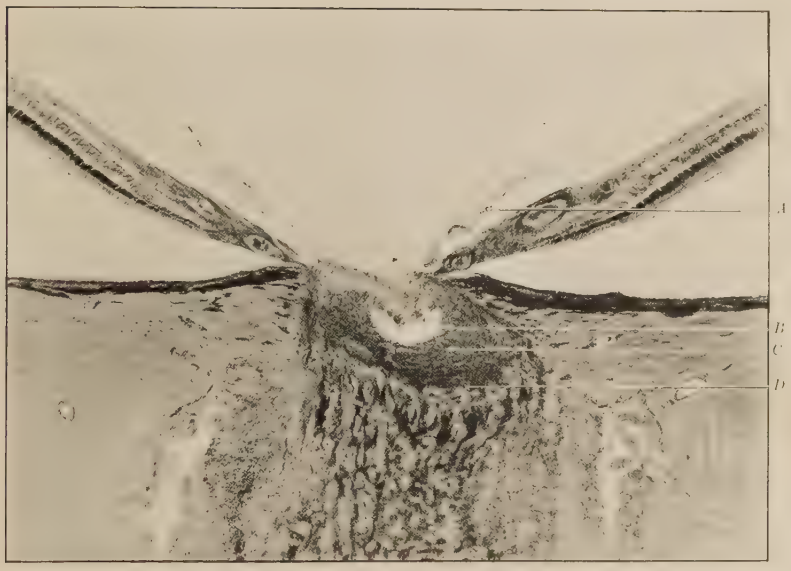


FIG. 1.

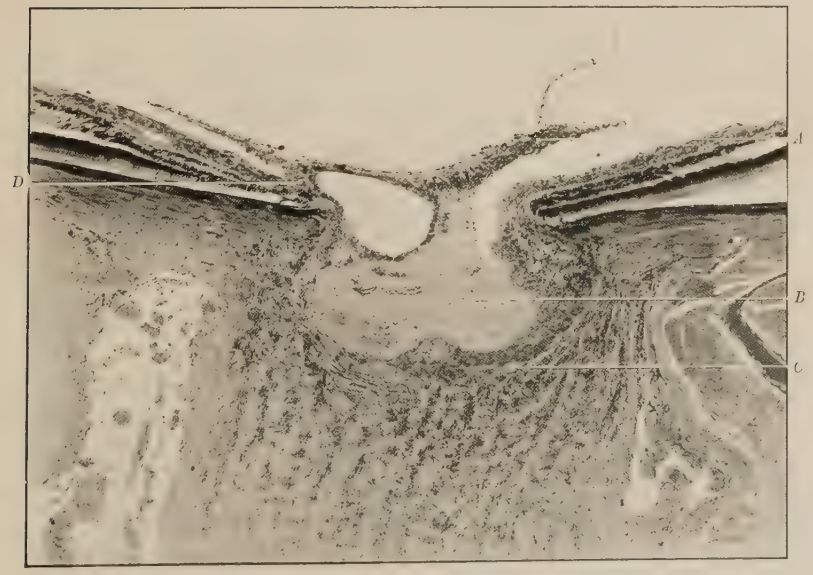


FIG. 2

Bale & Danielsson, Ltd.

Description of Plates X and XI, Figs. 1 to 4.

Fig. 1.—A case of iridocyclitis of doubtful duration, followed by secondary glaucoma. The cup is full of fibrous tissue (C) stretching out over the surface of the retina in the form of wings (A). The connective tissue in the cup is in an early stage of stretching, and a space is being formed in the centre of the mass (B). Lamina cribrosa is situated at D.

Fig. 2.—A similar case to that shown in Fig. 1, the inflammation having probably extended over a period of nearly 20 years. The mass (B) filling the glaucoma cup sends wings over the retina on each side (A), and at one part it shows an attachment to the degenerated retina (D), thus indicating an early stage in the process of dragging down. Lamina cribrosa is shown at C.

Fig. 3.—A section of a glaucoma cup from an eye which had been struck with a stone 19 years before removal, causing a detachment of the retina. The fibrous tissue formed in the cup is attached loosely to the degenerated retina above (A), and has become so stretched that large spaces have resulted. These spaces often contain blood or coagulated material. D. Piece of fibrous tissue lying free. C. Lamina cribrosa.

Fig. 4.—A section of the glaucoma cup from an eye which was struck by a boot 4 years before removal. In this case the retina has been dragged down almost into the cup, but just below the edge the uniting strand is in the act of giving way, unable to withstand the pull which the receding cup has put upon it.

A. Retina.
B. Stretched retinal tissue.
C. Fibrous band.
D. Lamina cribrosa.

Name.	Age.	Surgeon.	Eye.	History.
(1) J. W.	4	Mr. Lang. Dec. 2, 1901.	L.	Ophthalm ianeonatorum. Eye inflamed ever since.
(2) Jessie R. ...	68	Mr. Spicer. Jan. 22, 1902.	L.	Two years ago injury. Attended R. L. O. H. ever since.
(3) George P. ...	60	Mr. Lawford. Feb. 8, 1902.	L.	O. P. since 1897.
(4) Wm. F. ...	50	Mr. Gunn. Mar. 29, 1902.	L.	O. P. 11.12.01. Had left inflamed 3 weeks previously.
(5) Elizabeth D. ...	66	Mr. Silcock. June 10, 1902.	R.	19.11.01. R. Idy. much inflamed. 10.2.02. Accidentally rubbed. Never well since.
(6) Eliza J., ...	68	Mr. Lawford. June 11, 1902.	R.	Sight of right failed slowly in a few months. Blind 12 months.
(7) Edmund M. ...	75	Mr. Lang. June 16, 1902.	R.	Feb., 1902. R. became inflamed after a fall.
(8) Maria J. ...	69	Mr. Lawford. June 21, 1902.	L.	In 1905. L. extraction; 7 months later a needling.
(9) Frances C. ...	70	Mr. Gunn. July 23, 1902.	L.	4.11.99. L. Idy. 24.1.00. L. extraction. 12.1.01. L. needling. L. eye never comfortable since needling.
(10) Fk. K. ...	61	Mr. Lang. Nov. 12, 1902.	L.	Fifteen weeks ago kick from a horse. Operation 3 weeks ago.
(11) Mary D. ...	58	Mr. Spicer. Nov. 15, 1902.	L.	28.6.99. O. P. with chronic glaucoma. Blind 1½ years ago.
(12) Mary W. ...	61	Mr. Silcock. Dec. 13, 1902.	L.	Twenty years ago inflammation in left (?). At this time an Idy. performed in right.
(13) Emily S. ...	30	Mr. Gunn. Dec. 20, 1902.	R.	7.4.97. R. extraction. 5.7.97. R. needling. Capsule got adherent to wound. 7.7.97. Idy. to relieve tension.
(14) Sarah S. ...	70	Mr. Gunn. Dec. 24, 1902.	L.	Left eye "bad" for 18 years.

Clinical condition.	Onset of glaucoma.	Pathological examination.
Intercalary staphyloma and iritis.	... ...	Retina degenerated. Fibrous tissue in cup.
Iritis and iridocyclitis.	Increased tension off and on for 18 months.	Arteriosclerosis. O. D. cupped, and full of fibrous tissue.
Extensive choroiditis. Round patch just above disc, which appears filled in.	Painful and increased tension 9 months.	Retina very atrophic, two calcareous masses near the disc. Much nuclear connective tissue in cup.
Pannus, iritis.	Painful and increased tension for 3 months.	New fibrous tissue in the optic cup.
Iris caught up in wound. Vesicular keratitis. Some fine K. P.	?	Vessels atheromatous. Small amount of fibrous tissue in cup.
Probably a case of chronic glaucoma.	Painful and increased tension for 4—5 weeks.	Cup filled with new fibrous tissue.
Inflammation for 2 months, producing iritis with post-synechiæ.	?	Small amount of fibrous tissue in cup.
Repeated attacks of iridocyclitis.	Had pain in left probably for some time, but no note as to how long.	Cystoid cicatrix. O. D. full of fibrous tissue.
Evidences of iridocyclitis. K. P. Vitreous opacities.	?	*No* cup, but retina heaped up and folded near the disc.
Bulging scar at upper sclero-corneal margin. Iris adherent. Dislocated lens.	Tension was +3 when removed.	Retina degenerated. Fibrous tissue lining optic cup.
Some K. P. Evidence of old iritis.	Glaucoma (chronic for 3 years).	Optic cup filled with fibrous tissue, which sends wings out over the retina.
? Sympathetic ophthalmia; evidence of iridocyclitis; fine K. P. in left.	?	Optic cup filled with fibrous tissue, which sends wings out over the retina.
Some iris got caught up in wound, with resulting inflammatory reaction.	Pain and tension for 3 weeks, but some tension 4 years ago.	Optic cup full of fibrous tissue containing leucocytes.
Keratitis. Old iritis with synechiæ.	Blind 3 months.	Optic cup full of fibrous tissue, which contains dilated spaces.

Name.	Age.	Surgeon.	Eye.	History.
(15) Letitia G. ...	50	Mr. Lang. Feb. 23, 1903.	R.	?
(16) John F. ...	60	Mr. Flemming. Mar. 7, 1903.	L.	Eight weeks previously injured with stone.
(17) Jas. P. ...	28	Mr. Lawford. Mar. 14, 1903.	L.	Said to be blind since birth. 15 month ago, blow on temple. Eye painf since.
(18) James W. ...	70	Mr. Gunn. Mar. 28, 1903.	L.	Thirty years ago detached retina. years ago attack of glaucoma in left.
(19) Mary B. ...	75	Mr. Silcock. Apr. 21, 1903.	L.	Twelve or 14 years ago inflamed.
(20) Jas. D. ...	40	Mr. Gunn. Apr. 22, 1903.	R.	17.12.98. O. P., with recurrent iritis. July, 1902. Had rheumatic gout, fo lowed by iritis.
(21) Ellen C. ...	33	Mr. Lang. Apr. 30, 1903.	R.	Injured by a stone when 6 years old.
(22) Caroline R. ...	55	Mr. Morton. May 5, 1903.	R.	Left eye first bad 3 years ago. 8 month ago L. failed, with much pain. operated on several times.
(23) Maud E. ...	17	Mr. Marshall. Nov. 27, 1903.	L.	Ten years ago had ulcers. Not been ab to see since.
(24) Ellen W. ...	53	Mr. Silcock. Feb. 16, 1904.	R.	Five years ago sight of right began get dim; was red and inflamed; hom in 1903, when doctor did Idy.
(25) Bessie B. ...	37	Mr. Spicer. Feb. 18, 1904.	L.	"Was bad" 3 months ago with inflam mation. 18 years ago struck wit champagne cork. O. P. in 1885 wit detached retina.
(26) Annie B. ...	65	Mr. Fisher. Mar. 16, 1904.	R.	Four years ago sight of right suddenl lost, with great pain. 1 week ago re and painful.
(27) Alfred S. ...	62	Mr. Lawson. Oct. 4, 1904.	R.	Eye bad since Aug., 1904.

* Parsons, Trans. Oph

Clinical condition.	Onset of glaucoma.	Pathological examination.
Myopia. Patches of choroiditis. Evidence of chronic iritis.	?	Optic cup filled with fibrous tissue, which contains spaces full of blood.
Keratitis. Iritis. Iris bombé.	?	Much fibrous tissue in optic cup.
Iridocyclitis.	Painful for 15 hours.	Not much fibrous tissue in cup, but folded degenerated retina near disc.
Ulceration of cornea. Hypopyon. T. +. No P. L.	Blind for 3 years.	Fibrous tissue in optic cup distended to form spaces.
Large corneal scar with iris adherent.	Pain. Blind for 1 month.	Small amount of fibrous tissue in optic cup.
Evidences of old iritis. T. + 1. No P. L.	Sight began to fail 5 months ago. Blind for 2 months.	Optic cup filled with cystic retina.*
Keratectasia, calcareous band of cornea. Iritis. No. P. L.	Painful for 3 weeks.	Optic cup contains many strands of fibrous tissue.
? Sympathetic. Evidence of iridocyclitis. Much K. P.	... ...	Optic cup full of fibrous tissue, sending wings over retina.
Buphthalmic. Corneal nebulæ.	Painful for 3 weeks.	Choroido-retinitis. Optic cup contains small amount of fibrous tissue.
Much acute inflammation. Iris adherent to corneal wound. T. +3. No P. L.	... ...	Optic cup contains much infiltrated fibrous tissue.
Corneal ulcer. Bombé iris. T. +2. No P. L.	Three months painful.	Retina detached and degenerated. Optic cup filled with new fibrous tissue, sending out endothelial membrane over retina.
Hypopyon ulcer.	... ...	Optic cup filled with fibrous tissue, spreading out into vitreous.
Acute iritis. T. +2. No P. L.	?	Retinal hæmorrhage. Optic cup partly filled up with fibrous tissue.

Soc., 1905, p. 99.

Name.	Age.	Surgeon.	Eye.	History.
(28) Emily B. ...	52	Mr. Collins. Oct. 24, 1904.	R.	Six months ago eye was red and painful; then worse 1 month ago.
(29) Emma M. ...	38	Mr. Lang. Feb. 27, 1905.	R.	Always divergent, and amblyopic. Inflammation 1½ years, and again 6 months ago.
(30) John R. ...	55	Mr. Lawford. May 27, 1905.	L.	Gradual failure of sight in left eye for 9 years without pain or tenderness.
(31) John M. ...	77	Mr. Lang. June 9, 1905.	R.	Struck by a boot 4 years ago. 2½ years ago went blind gradually without pain.
(32) Thos. R. ...	58	Mr. Spicer. Aug. 11, 1905.	R.	Ten years ago struck by stone, followed by detachment of retina.

Bibliography.

(1) Schnabel. Arch. f. Augenheilk., vol. xxiv, 1892.
(2) Axenfeld. IXe Congrès International D'Ophtalmologie, 1899, p. 112.
(3) Krukenberg. Klin. Monatsbl. f. Augenheilk, vol. xxxviii, Beilageheft, p. 47, 1900.
(4) Roscher. Klin. Monatsbl. f. Augenheilk., vol. xxxix, 2, p. 947, 1901.
(5) Gama Pinto. Arch. f. Ophth., vol. xxviii, 1, p. 170, 1882.
(6) Kampherstein. Klin. Monatsbl. f. Augenheilk., vol. xli, pt. i, p. 25, 1903.

Clinical condition.	Onset of glaucoma.	Pathological examination.
T. + 3. No P. L.	?	Retina shows hæmorrhages. Optic cup partly filled with fibrous tissue.
Bullous and filamentous keratitis. Bombé iris. T. +2. No P. L.	Painful for several months.	Retina degenerated, and shows much new-formed connective tissue. Retina attached by strand to bottom of glaucoma cup.
Cornea hazy; no A. C. Iris attached to back of cornea. Lens shrunken and opaque. No P. L. T. +2.	Red and painful for 4—5 weeks.	Atrophic iris wholly adherent to cornea. Leucocytes in vitreous. Optic cup contains fibrous tissue stretched to form spaces which are full of blood.
Transverse band of corneal opacity. Lens dislocated and opaque. T. +3. No P. L.	Painful for 2 months.	Iris bound down and infiltrated; ciliary body also infiltrated. Fibrous tissue in optic cup stretched to form spaces.
Large irregular staphyloma of sclerotic in equatorial region. T. +1.	?	Retina detached and folded. Attached by strand to bottom of optic cup.

(7) Ginsberg. Pathologische Histologie des Auges, p. 464, 1903.
(8) Parsons. Folding of Retina in Glaucoma Cup, Trans. Ophth. Soc., vol. xxv, p. 99.
(9) Parsons. Pathology of the Eye, vol. ii, p. 575.
(10) Paton. Folded Retina at Optic Disc, Trans. Ophth. Soc., vol. xxiii, p. 63, 1903.
(11) Parsons on Paton's case, Trans. Ophth. Soc., vol. xxiv, p. 149.
(12) Baquis. La trombosi della vena centrale della retina. Festschrift für Julius Hirschberg, p. 33, Figs. 6 and 8.

INDEX TO VOL. XVI.

PAGE

Accommodation, development of 123
Albuminuric retinitis (in young subjects) 1
Analysis of a series of consecutive cases of conjunctivitis seen in Aberdeen 434

Blepharitis marginalis 307

Capsular complications after cataract extraction 247
Cataract, heredity in 179
Cataract complications after extraction 247
Central artery, obstruction of 262
Central vein, thrombosis of 62
Cerebrospinal meningitis, metastatic ophthalmia in 565
Chancre of conjunctiva (with interstitial keratitis) 16
COATS, GEORGE—
A case of tubercle of the nerve head 381
Obstruction of the central artery of the retina 262
The structure of the membrane of Bruch and its relation to the formation of colloid excrescences 164
Thrombosis of the central vein of the retina 62
Further cases of thrombosis of the central vein of the retina 516
COLLINS, E. TREACHER—
Capsular complications after cataract extraction 247
Development of the accommodative power of the human lens 123
Primary chancre of the conjunctiva and interstitial keratitis 16
Colloid degeneration of conjunctiva 135
Colloid excrescences of the membrane of Bruch 164
Conjunctiva—
Chancre of 16
Colloid (hyalin) degeneration of 135
Implantation dermoid of 318
Ossification of 139
Papilloma of 370
Petrifaction of 139

PAGE

Conjunctivitis—
Angular ... 307
Bacteriology of ... 307, 463

Ehrlich's theory of immunity in its relation to ophthalmology ... 415

Foreign body (wood) under conjunctiva ... 318
Fovea, opacity in ... 410
Fraser. See Usher and Fraser.

Glaucoma—
Following thrombosis of central vein ... 110, 555
Retina in cup in ... 574
Glioma retinæ ... 323
Glioma retinæ in shrunken globe ... 141

Hancock, W. Ilbert—
A case of (?) tubercle of the retina ... 150
Ring scotoma ... 496
Hepburn, M. Langton—
Retina in glaucoma cup ... 574
Herbert, H.—
Two cases of colloid (hyalin) degeneration of the tarsus and conjunctiva ... 135
Heredity in cataract ... 179, 389
Hyalin degeneration of the conjunctiva ... 135

Implantation dermoid of conjunctiva ... 318
Immunity in relation to ophthalmology ... 415
Interstitial keratitis following chancre of the conjunctiva ... 16

Lens, development of accommodative power in ... 123

Macnab, Angus—
Marginal blepharitis ... 307
Mayou, M. S.—
Implantation dermoid of conjunctiva ... 318
Intradural tumour of the optic nerve. Neurofibromatosis ... 155
Metastatic infection of the eye, associated with—
(*a*) Cerebrospinal meningitis ... 565
(*b*) Typhoid fever ... 569

Membrane of Bruch, structure of ... 164

PAGE

Metastatic infection from—
Cerebrospinal meningitis 565
Typhoid fever 569
Morax-Axenfeld diplobacillus 314, 463
Myopia 410

NETTLESHIP, E.—
Extensive congenital opacity of retina in yellow spot region, etc. ... 410
Heredity in the various forms of cataract 179
Additional cases of hereditary cataract 389
Observations on the prognostic and diagnostic value of retinitis in diabetes 11
Renal retinitis in young subjects, etc. 1
Neurofibromatosis of optic nerve 155

Obstruction of the central artery of the retina 262
Opaque nerve fibres 410
Optic nerve—
Intradural tumour of 155
Tubercle of 381
OWEN, S. A.—
Glioma retinæ 323

Papilloma limbi conjunctivæ 370
PARSONS, J. HERBERT—
Case of glioma in a shrunken globe 141
Ehrlich's theory of immunity in its relation to ophthalmology 415
Innervation of the pupil 20
PASCHEFF, C.—
Papilloma limbi conjunctivæ 370
Pupil, innervation of 20

Retina—
In glaucoma cup 574
Glioma 323
Glioma in shrunken globe 141
Obstruction of central artery of 262
Opacity in yellow spot region 410
Thrombosis of central vein of 62, 516
Tubercle of 150, 381
Retinitis—
Albuminuric (in young subjects) 1
Diabetic (prognostic and diagnostic value of) 11
Hæmorrhagic 62, 516
Ring scotoma 496

PAGE
Thrombosis of the central vein of the retina..... 62, 516
Tubercle of nerve head 381
Tubercle of retina 150
Typhoid fever, metastatic ophthalmia in 569

Usher, C. H., and Fraser, H.—
Analysis of a series of consecutive conjunctivitis cases seen in Aberdeen 434

Harrison & Sons, Printers in Ordinary to His Majesty, St. Martin's Lane.